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FEATURING TREATMENT

Treatment! . . . treatment! . . . treatment! . . . as detailed in the *Medical Clinics of North America* number after number, year in and year out, is *one* of the reasons for the great and constantly increasing success of these unique books of postgraduate medicine.

The *March Number from Baltimore* exemplifies this. Its *11-clinic Symposium on Gynecology and Obstetrics* gives special attention to *Treatment.* For instance, there are clinics on *Treatment* of Pruritus Vulvae, *Treatment* of Vaginitis, *Treatment* of Acute Gonococcal Salpingitis, *Treatment* of Cystitis in the Female, *Office Treatment* of Cervicitis, Dysmenorrhea (including Clinical and Pharmacological Studies on Benzedrine Sulfate), Significance and *Treatment* of Menopausal Bleeding, Diagnosis and *Treatment* of Missed Abortion, *Treatment* of Eclampsia, *Treatment* of Hyperemesis Gravidarum, and Clinical Aspects of Twin Pregnancy. *Treatment* is the Keynote!

But the March Number, in *addition* to the Symposium, gives you many other clinics of special interest —clinics just as helpful, just as practical as those in the Symposium. *Here are a few of them: Treatment* of Acute Circulatory Failure, Management of Early Essential Hypertension, Diagnosis and *Treatment* of Lesions of Small Bowel, Diagnosis and Management of Diarrheas and Dysenteries, *Treatment* of Insomnia, etc. Here, indeed, is postgraduate medicine . . . truly today's medical practice.

Full Details in SAUNDERS ADVERTISEMENT—Page 3

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TREATMENT OF PNEUMOCOCCIC PNEUMONIA WITH SULFANILAMIDE

ALVIN E. PRICE, M.D.
AND
GORDON B. MYERS, M.D.
DETROIT

Sulfanilamide has proved bacteriostatic against types I, II, III and XIV pneumococci in vitro and in laboratory animals, according to various authors.[1] While the drug probably has been used widely for human pneumococcic pneumonia, the reports to date are meager. Heintzelman, Hadley and Mellon [2] used it in nine cases of type III pneumonia and obtained seven recoveries, whereas among ten controls there were only two recoveries. Millett [3] reported one case of type III pneumonia in which a crisis occurred after the use of sulfanilamide. Louis [4] added six cases of pneumococcic pneumonia in which recovery occurred with sulfanilamide therapy.

The following report is based on 115 patients treated with sulfanilamide,[5] compared with forty patients receiving serum and ninety-four controls receiving identical symptomatic and supportive measures but no specific therapy. While this series is too small to be statistically significant, it is reported in the hope that an evaluation of the drug in the treatment of pneumonia may eventually be made by combining it with cases studied elsewhere.

METHOD OF STUDY

Diagnosis.—The diagnosis was confirmed by roentgenogram in every case. The admission sputum was typed directly by the Neufeld method, and the results were checked either by mouse inoculation or by the direct typing of a second specimen. Typing was repeated in the event of an extension. Blood for culture was taken on admission and cultures were repeated daily if positive. Hemoglobin estimations, white cell counts and differential counts were made daily during sulfanilamide therapy and at frequent intervals for the controls. Red cell counts were made twice weekly. Serum agglutinins were determined during convalescence.

Selection of Cases.—All patients over 12 years of age with pneumonia due to a single type of pneumococcus who were admitted between Oct. 1, 1937, and July 1, 1938, and remained in the hospital at least twenty-four hours were included in this study. Children under 12 were excluded because childhood and adult pneumonias are not strictly comparable. Patients who were moribund on admission and died within twenty-four hours were excluded because it was felt that they did not provide a fair trial of any form of therapy. Eight such patients were treated with sulfanilamide, three with serum and eight as controls. Two other patients treated as controls for three and six days respectively, with sulfanilamide therapy started within eight hours of death, were excluded from the tabulations.

Alternate patients with types I, II and VII pneumonia were treated with sulfanilamide and Felton serum, a few being reserved as controls. With types V and VIII pneumonia, serum was available for only a portion of the patients alternated with those receiving sulfanilamide. With the remaining types, patients receiving sulfanilamide were alternated with controls, who received similar symptomatic and supportive treatment. If for any reason the type could not be determined promptly, the patient was classed tentatively among those having nonpneumococcic pneumonia, who likewise were treated alternately with sulfanilamide. For several of these patients the type of invading pneumococcus was subsequently determined, thus causing discrepancies in the total number of patients treated by the two methods.

Dosage of Sulfanilamide.—The oral route was used as a routine, subcutaneous injections being substituted with those too ill to take or retain the drug by mouth. An initial massive dose of 15 grains (1 Gm.) to 20 pounds (9 Kg.) of body weight was given to all patients, those over 160 pounds (73 Kg.) receiving the maximum dose of 120 grains (8 Gm.). A similar total (15 grains to 20 pounds) was administered during the next twenty-four hours, divided into six equal doses, the first given four hours after the initial massive dose and the remainder at intervals of four hours around the clock. An equal amount of sodium bicarbonate accompanied each dose of sulfanilamide. The blood sulfanilamide

This study was aided in part by a grant from the Commonwealth Fund.

From the Medical Department of the City of Detroit Receiving Hospital and Wayne University College of Medicine.

1. These include:
Rosenthal, S. M.: Chemotherapy of Experimental Pneumococcus Infections, Pub. Health Rep. **52:** 48 (Jan 8) 1937.
Gross, Paul, and Cooper, F. B.: P-Aminobenzenesulfonamide and Antipneumococcal Serum Therapy in Type I Pneumococcal Infections in Rats, Proc. Soc. Exper. Biol. & Med. **36:** 535 (May) 1937.
Kreidler, W. A.: Treatment of Pneumococcal Infections in Rabbits with Sulfanilamide, ibid. **37:** 146 (Oct.) 1937.
Cooper, F. B., and Gross, Paul: Sulfanilamide, Antipneumococcus Serum and Vitamin C Therapy in Type II Pneumococcal Pneumonia of Rats, ibid. **36:** 774 (June) 1937.
Cooper, F. B.; Gross, Paul, and Lewis, M.: Chemotherapy of Pneumococcal (Type II) Meningitis in the Rat, ibid. **38:** 835 (June) 1938.
Cooper, F. B.; Gross, Paul, and Mellon, R. R.: Action of P-Aminobenzenesulfonamide on Type III Pneumococcus Infections in Mice, ibid. **36:** 148 (March) 1937.
Cooper, F. B., and Gross, Paul: P-Aminobenzenesulfonamide Therapy in Experimental Type III Pneumococcal Pneumonia, ibid. **36:** 678 (June) 1937.
Schmidt, L. H.: Use of Sulfanilamide in Treatment of Type XIV Pneumococcus Infections in Mice, ibid. **37:** 205 (Oct.) 1937.

2. Heintzelman, J. H. L.; Hadley, P. B., and Mellon, R. R.: Use of P-Aminobenzenesulfonamide in Type III Pneumococcus Pneumonia, Am. J. M. Sc. **193:** 759 (June) 1937.

3. Millett, Joseph: Sulfanilamide: Report of a Case, New York State J. Med. **37:** 1743 (Oct. 15) 1937.

4. Louis, D. J.: The Treatment of Pneumonia with Sulfanilamide, Illinois M. J. **73:** 422 (May) 1938.

5. The sulfanilamide was furnished by Merck & Co.

level was determined within the first twenty-four hours and daily thereafter. An attempt was made to keep the blood concentration between 7 and 15 mg. per hundred cubic centimeters but preferably above 10 mg. As long as it was within this range, 15 grains to 20 pounds divided into six equal doses was given during each subsequent twenty-four hour period. If the blood level did not reach 7 mg. per hundred cubic centimeters, either the subcutaneous route was substituted or a larger dose was given by mouth. In most instances administration of the drug was discontinued after the temperature had been normal for twenty-four hours. If blood levels were maintained between 7 and 15 mg. per hundred cubic centimeters for five days without definite clinical response the case was classed as a therapeutic failure and the drug therapy was stopped. At the advent of serious toxic manifestations, particularly jaundice and changes in the blood picture, treatment with sulfanilamide was discontinued and transfusions were given.

Treatment of Patients Receiving Serum and of Controls.—This treatment was similar to that described by one of us (A. E. P.[6]) in a previous communication, except that serum was given in larger doses at intervals of two hours. The average total dose for type I pneumonia was 210,000 units; for type II, 255,000; for type V, 124,000; for type VII, 175,000, and for type VIII, 110,000 units.

TABLE 1.—*Summary of Cases*

	Patients Treated with Sulfanilamide										Controls and Patients Treated with Serum									
Type	Number of Cases	Average Age	Chronic Alcoholism	Average Duration Before Therapy, Hours	Average Number of Lobes Consolidated	Extension	Bacteremia	Good Therapeutic Response	Average Time Until Therapeutic Response, Hours	Number of Deaths	Form of Treatment	Number of Cases	Average Age	Chronic Alcoholism	Average Duration Before Therapy, Hours	Average Number of Lobes	Extension	Bacteremia	Average Time Until Therapeutic Response, Hours	Number of Deaths
I	11	36	2	90.4	1.5	2	2	9	49	1	C.	6	41	2	122	2.3	1	2	132	3
											Ser.	10	32.3	1	69.3	1	3	4	36	0
II	18	42.8	6	100	1.5	3	3	14	53.3	3	C.	6	35.5	1	106.8	1.1	0	3	101.3	3
											Ser.	14	39.4	3	46.2	1.2	2	5	56	6
III	5	40	1	62.4	1.6	0	1	2	27	3	C.	9	65.6	0	77.4	1.3	0	2	88	6
IV	9	38.3	4	113.1	1.7	3	2	5	55.6	1	C.	5	50	2	189	1.4	0	1	96	2
V	11	37	3	74.9	1.1	2	2	11	48.4	0	C.	6	47	3	86	1	0	1	201.6	1
											Ser.	5	41.2	1	80	1	0	0	18.6	0
VI	3	53	1	56	1	0	1	2	52	1	C.	2	64.5	1	48	3.5	0	0	.....	2
VII	10	38.2	3	126.8	1.3	2	1	5	67.8	1	C.	3	52.3	0	38	2.3	0	0	64	0
											Ser.	9	45.4	3	60.3	1.4	1	3	65.2	5
VIII	7	33.4	1	77.8	1.4	0	0	6	45	1	C.	6	46	1	46.5	1.3	0	0	66	0
											Ser.	2	54	1	40	1	0	0	36	0
IX	1	35	1	48	3	0	0	1	84	0	C.	4	29.5	1	31	1.7	1	0	96	1
X	1	42	0	120	1	0	0	0	....	0	C.	1	77	1	0	1	1	0	192	0
XI	0										C.	1	12	0	0	1	0	0	.....	0
XII	5	33.4	0	105.2	2	0	1	5	49.8	0	C.	4	40	1	24.5	1	0	1	67	0
XIII	0										C.	1	36	0	72	2	0	0	4	0
XIV	4	29	2	138.2	2	0	4	3	64	0	C.	2	39	0	60	1	1	0	144	1
XV	3	34.7	2	64	1.3	0	0	3	56	0	C.	3	44.7	1	11.3	1	1	0	84	0
XVI	2	50	0	81	1	0	0	2	24	0	C.	2	37	0	72	2	0	0	72	0
XVII	4	39.5	2	87.2	1.5	0	0	3	23	1	C.	3	53	1	16	2.3	1	0	72	1
XVIII	3	36	2	65	1.7	0	0	2	15	1	C.	6	41	1	68	1.5	0	0	82.8	1
XIX	5	35.4	0	109.4	1.2	0	2	4	70	1	C.	6	44	0	32	1.8	0	1	168	2
XX	2	48	1	60	1.5	0	0	1	12	1	C.	3	50.6	0	52	1.3	0	1	84	1
XXI	1	36	0	24	1	0	0	1	48	0	C.	0								
XXII	0										C.	2	52	2	182	2.5	1	0	.....	2
XXIII	1	12	0	144	1	0	0	1	48	0	C.	1	66	0	86	1	0	1	168	0
XXIV	2	45	0	66	3	0	0	2	65.5	0	C.	1	47	1	96	1	0	0	120	0
XXV	2	48	0	126	3.5	0	1	1	120	1	C.	3	27	1	61	1.3	0	1	60	1
XXVIII	2	41	2	31.5	2	0	0	1	11	1	C.	2	27	0	36	1.5	0	0	60	0
XXIX	1	49	1	65	1	0	0	1	25	0	C.	4	46	2	96	2	0	1	18	2
XXXI	1	36	0	48	1	0	0	0	....	0	C.	1	52	0	144	2	0	0	72	0
XXXII	1	59	1	168	2	0	1	0	....	1	C.	1	49	0	0	1	1	0	120	0
	115	38.7	35	92.0	1.53	12	21	85	50.3	18	C.	94	45.6	22	71.7	1.51	8	15	98.9	29
											Ser.	40	39.9	9	59.1	1.16	6	12	42.5	11

TABLE 2.—*Effect of Sulfanilamide on Temperature*

Blood Sulfanilamide Level at the Time Temperature Level Fell to Normal	Hours Between Commencement of Sulfanilamide Therapy and Defervescence									Maximal Blood Sulfanilamide Level	No Response to Sulfanilamide		Totals
	0-11	12-23	24-35	36-47	48-59	60-71	72-83	84-95	96-120		Recovered	Died	
Below 4 mg. per 100 cc.	0	0	0	2	0	0	0	0	0		0	0	2
4- 6.9 mg. per 100 cc...	2	0	0	1	0	1	1	1	0		4	1	11
7- 9.9 mg. per 100 cc...	4	4	5	6	3	1	3	2	3		4	7	42
10-12.9 mg. per 100 cc...	3	4	3	5	2	1	3	2	3		3	4	35
13-15.9 mg. per 100 cc...	4	3	1	2	1	0	0	0	1		0	3	15
16-21 mg. per 100 cc.....	0	0	0	0	0	0	0	0	0		1	3	4
Not determined.....	0	2	0	0	1	0	0	1	2		0	0	6
Totals.....	13	13	9	16	7	3	7	6	11		12	18	115

SUMMARY OF CASES

Race, Sex and Age.—Most of the significant data for the sulfanilamide, serum and control groups have been summarized in table 1. The racial distribution was as follows: sulfanilamide group, white 63.5 per cent and Negro 36.5 per cent; serum group, white 72.5

6. Price, A. E.: Modern Treatment of Pneumonia, J. Michigan M. Soc. **36**: 77 (Feb.) 1937.

per cent and Negro 27.5 per cent; controls, white 67 per cent and Negro 33 per cent. The proportion of males in the sulfanilamide group was 80.9 per cent, in the serum-treated group 82.5 per cent and in the controls 77.7 per cent. The age distribution was not as even as desirable, the average for the sulfanilamide group being 38.7 years as compared with 39.9 years for the serum-treated patients and 45.6 years for the controls.

Associated Diseases.—A history of daily consumption of alcohol was obtained from 30.4 per cent of the patients treated with sulfanilamide, from 22.5 per cent of those treated with serum and from 23.4 per cent of the controls. The Kahn reaction of the blood was positive for 23.5 per cent, 10 per cent and 14.9 per cent respectively. In the sulfanilamide group there was one patient with recent coronary thrombosis and four patients with congestive heart failure. The failure was secondary to hypertension in one, coronary sclerosis in two and syphilitic heart disease in one. There were four additional patients with definite clinical evidence of heart disease which remained compensated throughout their hospital stay. One of the patients treated with serum had failure of the right ventricle secondary to rheumatic mitral stenosis; another had well compensated mitral stenosis. Among the controls there were four patients with congestive heart failure secondary to hypertension and four others with compensated hypertensive or arteriosclerotic heart disease. Two controls and two of the patients treated with sulfanilamide had chronic asthmatic bronchitis. One of the patients treated with sulfanilamide had a compound fracture complicated by osteomyelitis, which was an important contributory factor toward his death. One of those in the control group had a carcinoma of the colon. The remainder had no associated diseases which were likely to affect the prognosis.

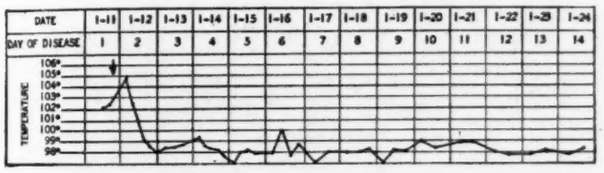

Chart 1.—Temperature in case 1.

TABLE 3 (case 1).—*Prompt Crisis Following the Use of Sulfanilamide, Type VII Pneumonia*

Patient a white youth aged 17; onset 8 p. m. January 10, admission January 11 and discharge Jan. 24, 1938.

Day of Disease	Sulfanilamide, Dose in Grains	Blood Level in Mg. per 100 Cc.	Blood Picture				Blood Culture	Agglutination	Miscellany
			Hb.	R.B.C.	W.B.C.	NF-F%			
1	140	8.7	....	....	.....	.....	Neg.	....	X-ray, consolidation of R.M.L. and portion of R.L.L.
2	120	8.1	12.5	4.99	38,000	65-32	.....	....	
3	120	8.6	12.5	....	20,100	61-33	.....	....	
4	60	8.2	....	....	.....	.....	.....	....	
5	...	4.3	11.5	....	10,400	37-48	.....	....	
8	...	...	....	....	.....	.....	.....	1:10	X-ray, considerable resolution
9	...	...	13.0	....	8,400	30-52	.....	....	
14	...	...	12.5	4.13	.....	.....	.....	....	

Duration and Extent of Pneumonia.—The average duration of the pneumonia before treatment was ninety-two hours in the sulfanilamide group, 59.1 hours for the serum-treated patients and 71.7 hours for the controls. The average number of lobes consolidated, as determined from the admission roentgenogram, was 1.53 in the sulfanilamide group, 1.16 in the serum group and 1.51 in the controls. The incidence of bacteremia was 19.1 per cent in the sulfanilamide group, 30 per cent for those treated with serum and 14.7 per cent for the controls. The admission leukocyte count was below 7,000 for four patients of the sulfanilamide group, for three serum-treated patients and for nine controls, and between 7,000 and 10,000 for twelve, four and eighteen patients, respectively.

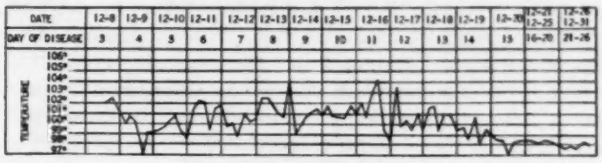

Chart 2.—Temperature in case 2.

TABLE 4 (case 2).—*Sulfanilamide Failure, Type IV Pneumonia with Bacteremia*

Patient a Negro aged 36; admission December 8 and discharge Dec. 31, 1937.

Day of Disease	Sulfanilamide, Dose in Grains	Blood Level in Mg. per 100 Cc.	Blood Picture				Blood Culture	Icteric Index	Miscellany
			Hb.	R.B.C.	W.B.C.	NF-F%			
3	120	...	13.6	4.4	6,800	33-55	IV	..	X-ray, pneumonia L.L.L.
4	120	15.6	11.4	3.79	9,250	86-8	Neg.	..	Liver extract 4 cc. 1 m. daily
5	120	9.9	11.8	....	20,700	87-8	.....	..	Sputum, type IV
6	120	11.0	12.2	....	40,600	.....	.....	..	
7	80	17.0	....	....	.....	.....	.....	..	
8	45	11.2	11.8	....	61,400	79-20	Neg.	38	X-ray, pneumonia L.L.L. and R.L.L.
9	30	8.2	10.2	3.34	27,700	70-28	.....	..	Sputum, type IV
10	0	4.1	10.6	....	41,000	71-28	.....	..	Urobilinogen in urine 1:300
11	0	0.9	....	....	.....	.....	Neg.	30	
12	0	0	....	....	.....	.....	.....	..	Urobilinogen 1:300
13	0	...	....	....	.....	.....	Neg.	..	X-ray, pneumonia R.L.L., R.U.L.; resolution L.L.L.
15	0	...	10.2	....	27,400	56-40	.....	10	Urobilinogen 1:50
21-26	0	...	9.6	....	8,000	20-67	.....	..	X-ray, slight resolution on right

RESULTS

Effect of Sulfanilamide on Temperature.—In table 2 the patients treated with sulfanilamide have been classed according to the number of hours elapsing between the commencement of the drug therapy and defervescence. The temperature fell to normal within twenty-four hours of the onset of sulfanilamide therapy in twenty-six cases (22.6 per cent), within forty-eight hours in fifty-one cases (44.3 per cent) and within 120 hours in eighty-five cases (73.9 per cent). On the other hand, the temperature reached normal within forty-eight

hours in only 16 per cent of the control cases. The effect of sulfanilamide on temperature was most striking when administration was started within thirty-six hours of the onset of the pneumonia. In fifteen of twenty-five such cases, the entire duration of the pneumonia, from onset to defervescence, was less than seventy-two hours. An example of an abortive crisis following sulfanilamide therapy is given in chart 1 and table 3 (case 1).

Twelve patients who did not show a temperature response within 120 hours but subsequently recovered from the pneumonia were classed as sulfanilamide failures. An example is given in chart 2 and table 4 (case 2). In this case, the blood culture became negative and a pseudocrisis occurred within twenty-four hours of the commencement of sulfanilamide therapy. In spite of adequate blood levels, the fever returned and the pneumonic process extended. The patient finally recovered, long after administration of the drug had been discontinued. Of the eighteen patients who died two had had a pseudocrisis, whereas the other sixteen showed no definite temperature response.

three of fifteen controls (20 per cent) and for seven of twelve patients (58.3 per cent) treated with serum. For those responding to sulfanilamide the blood culture usually became negative within twenty-four hours of the onset of therapy. The results were particularly good with type XIV, all four patients recovering. One of the most dramatic results is illustrated in chart 3 and table 6 (case 3). The patient was admitted on the seventh day of illness and was given no specific therapy during the first five days in the hospital. He showed roentgenographic evidence of an extension on the tenth day and positive blood cultures on the seventh, ninth, tenth and eleventh days. He was given a massive dose of sulfanilamide on the twelfth day and eight hours later had a crisis, eventually making a complete recovery. In chart 4 and table 7 (case 4) the course of type II pneumonia and bacteremia in a chronic alcoholic addict is illustrated. Sulfanilamide was started on the second day of illness. The blood culture was negative the following day and the temperature was normal from the fourth day. In chart 5 and table 8 (case 5) the course

TABLE 5.—*Results in Pneumococcic Bacteremia*

	Type of Pneumococcic Bacteremia															
	I	II	III	IV	V	VI	VII	XII	XIV	XIX	XX	XXIII	XXV	XXIX	XXXII	Total
Sulfanilamide																
Cases in which blood culture was positive	2	3	1	2	2	1	1	1	4	2	..	..	1	..	1	21
Cases in which blood culture became negative	2	2	0	2	2	0	0	1	4	2	..	..	1	..	1	17
Number of deaths	0	1	1	0	0	1	1	0	0	1	..	..	1	..	1	7
Controls																
Cases in which blood culture was positive	2	3	2	1	1	..	..	1	..	1	1	1	1	1	..	15
Cases in which blood culture became negative	1	0	0	0	0	..	..	1	..	0	0	1	0	0	..	3
Number of deaths	2	3	2	1	1	..	..	0	..	1	1	0	1	1	..	13
Serum																
Cases in which blood culture was positive	4	5	..	..	..	..	3	..	..	..	..	..	..	..	..	12
Cases in which blood culture became negative	4	3	..	..	..	..	0	..	..	..	..	..	..	..	..	7
Number of Deaths	0	3	..	..	..	..	3	..	..	..	..	..	..	..	..	6

In table 2 an attempt was made to correlate the temperature effect with the blood sulfanilamide level at the time of defervescence. No significant difference was noted between the group with blood sulfanilamide concentrations over 10 mg. per hundred cubic centimeters and the group with levels between 7 and 9.9 mg. When no therapeutic response occurred at low levels, larger doses were purposely given. One patient was observed who showed no improvement during three days when the blood level fluctuated between 4 and 7 mg. per hundred cubic centimeters but had a fairly prompt crisis after it rose to 10 mg. There were no definite examples of therapeutic failures at blood levels of from 7 to 9.9 mg. per hundred cubic centimeters followed by responses at higher levels. However, a much larger series will be needed to determine the optimal blood sulfanilamide concentration.

The effect of sulfanilamide on the pulse rate roughly paralleled that on the temperature. In some patients there was an associated symptomatic improvement but in many this was masked by the lassitude produced by the drug.

Effect of Sulfanilamide on Bacteremia.—The results in the cases of pneumococcic pneumonia complicated by bacteremia are given in table 5. For twenty-one of the patients treated with sulfanilamide the blood culture was positive on admission, and for seventeen (81 per cent) it became negative during treatment. On the other hand, the blood culture became negative for only

of type V pneumonia and bacteremia treated with sulfanilamide is illustrated. The blood was sterilized promptly and the temperature fell by lysis.

Five patients whose blood cultures became negative with treatment subsequently died. Three of these were in the sulfanilamide group, one in the serum group and one among the controls. In one of those whose blood culture became negative with sulfanilamide therapy hemolytic anemia subsequently developed, making it necessary to discontinue use of the drug. Ten days later the blood culture again showed the same organism and pneumococcic meningitis developed. At autopsy, it was seen that the pneumonia had completely resolved.

Effect of Sulfanilamide on the Consolidation.—Daily physical examinations were made to detect extensions and complications of the pneumonic process. The physical appearances were checked as often as necessary by x-ray examination. X-ray evidence of extension during sulfanilamide therapy was obtained in twelve cases (10.4 per cent), during serum therapy in six cases (15 per cent) and in eight control cases (8.5 per cent. Nine of the twelve patients in whom extensions developed during sulfanilamide therapy eventually recovered. The patients were also followed to determine the completeness of resolution. The consolidation cleared up in all but one of the patients classed as recovered. This patient still had evidence of unresolved pneumonia five months after sulfanilamide therapy had been discontinued. The effect of sulfanil-

amide on the sputum will be reported by Dr. Arthur W. Frisch in a separate communication.

Effect of Sulfanilamide on Complications.—The incidence of empyema was 1.7 per cent in the sulfanilamide group, 10 per cent for the serum-treated patients and

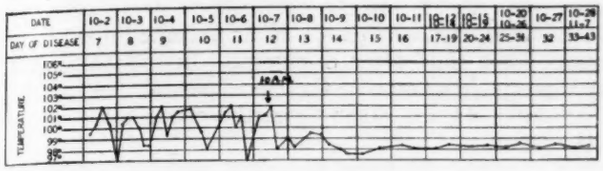

Chart 3.—Temperature in case 3.

TABLE 6 (case 3).—*Crisis Following the Use of Sulfanilamide, Type XIV Pneumonia and Bacteremia*

Patient a Negro aged 27; admission October 1 and discharge Nov. 7, 1937; delayed resolution.

Day of Disease	Oral Dose Sulfanilamide, Grains	Blood Level in Mg. per 100 Cc.	Blood Picture				Blood Culture	Miscellany
			Hb.	R.B.C.	W.B.C.	NF-F%		
7	...	...	12.6	4.45	33,000	84-14	XIV	X-ray, consolidation R.U.L.; sputum, type XIV
9	...	...	12.0	4.17	29,000	80-14	XIV	
10	...	...	....	....	.....	.....	XIV	X-ray, consolidation right lung
11	...	...	....	....	.....	.....	XIV	Very toxic
12	140	13	11.4	4.1	36,600	84-14	.....	Crisis after sulfanilamide
13	80	7	11.8	....	35,600	45-50	.....	Marked cyanosis
14	60	6.6	....	....	.....	.....	Neg.	
15	20	...	....	....	.....	.....	.....	Symptom free
16	...	...	11.6	....	24,300	65-24	.....	
17-19	...	...	10.8	3.6	23,400	51-39	.....	Icteric index 10; massive consolidation still present
20-24	...	...	11.8	4.6	17,000	36-55	.....	X-ray, consolidation and atelectasis
25-31	...	...	10.2	4.19	13,500	23-51	.....	Diathermy, right side of chest
32	...	...	....	....	.....	.....	.....	X-ray, considerable resolution
34-34	...	...	11.4	4.35	9,200	33-59	.....	Complete resolution

2.1 per cent for the controls. More frequent than empyema were small pleural effusions, which did not become purulent and eventually disappeared without surgical intervention. The incidence of these in the three groups was 4.3 per cent, 7.5 per cent and 5.3 per cent respectively. None of the patients in this series had lung abscess or pericarditis.

Effect of Sulfanilamide on Mortality.—The mortality rate for the 115 patients treated with sulfanilamide was 15.7 per cent and for the ninety-four controls was 30.8 per cent. The death rate in fifty-seven cases of types I, II, V, VII and VIII pneumonia treated with sulfanilamide was 10.5 per cent, whereas it was 27.5 per cent in forty cases of the same types treated with serum. While these figures are favorable to sulfanilamide, they are inconclusive because of the small number of cases, unevenly balanced as to type as well as to the following factors: The age distribution favored sulfanilamide. Likewise, the proportion of patients with leukopenia was lower in the sulfanilamide group. These factors were partly balanced by the longer average duration before treatment and the higher incidence of alcoholism, particularly delirium tremens, in the sulfanilamide group. The average extent of the consolidation was nearly equal in the sulfanilamide and control groups and considerably less in the serum group. The incidence of bacteremia was highest in the serum group and lowest in the controls.

The mortality for pneumonia complicated by bacteremia is given in table 5. The mortality rate was 33⅓ per cent for the patients treated with sulfanilamide, 50 per cent for those treated with serum and 86.6 per cent for the controls.

The results with type II pneumonia were particularly encouraging. Among eighteen patients treated with sulfanilamide there were 16.6 per cent of deaths, as compared with a mortality of 42.9 per cent for fourteen patients treated with serum. The results with the other types are given in table 1 and will not be discussed further because of the small number of cases of each type.

TOXIC MANIFESTATIONS

Cyanosis.—This developed in practically every patient treated with sulfanilamide. There was no apparent correlation between the depth of the cyanosis and the outcome in the case. Many patients with deep cyanosis made satisfactory recoveries. It has been shown that sulfanilamide cyanosis is usually due to blood pigmentation, less commonly to methemoglobinemia and rarely to sulfhemoglobinemia.[7] King and Leslie [8] were unable to demonstrate any significant reduction in oxygen saturation of the arterial blood during sulfanilamide therapy in eight cases.

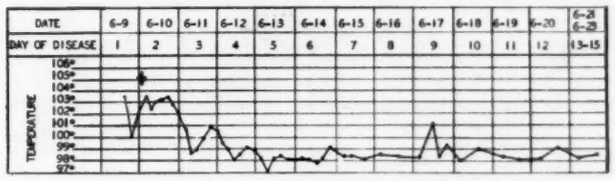

Chart 4.—Temperature in case 4.

TABLE 7 (case 4).—*Abortive Course of Type II Pneumonia and Bacteremia Following Sulfanilamide Therapy*

Patient a white man aged 47; onset 3 a. m. June 9, admission June 9 and discharge June 23, 1938; chronic alcoholism.

Day of Disease	Sulfanilamide, Dose in Grains	Blood Level in Mg. per 100 Cc.	Blood Picture				Blood Culture	Sputum	Miscellany
			Hb.	R.B.C.	W.B.C.	NF-F%			
1	0	....	10.0	....	19,000	15-74	Pos.	II	
2	240	10.3	9.5	3.45	17,300	46-43	.....	II	X-ray, consolidation R.L.L.
3	120	11.1	9.5	....	15,100	66-27	Neg.	..	Kline test pos., Kahn test pos.
4	120	....	....	....	.....	.....	.....	..	
5	60	13.1	10.5	3.66	9,900	50-38	.....	..	
6	0	....	....	....	.....	.....	.....	..	X-ray, consolidation with small pleural effusion
9	0	....	11.0	3.6	8,400	30-47	.....	..	
12	0	....	11.0	....	4,100	12-55	.....	..	
13-15	0	....	....	....	.....	.....	.....	..	Consolidation resolving, fluid disappearing

We are planning to repeat these studies on a larger scale with pneumonia, since it must be shown that

7. Marshall, E. K., and Walzl, E. M.: On Cyanosis from Sulfanilamide, Bull. Johns Hopkins Hosp. **61**: 140 (Aug.) 1937. Ottenberg, Reuben, and Fox, C. L.: Explanation for the Cyanosis of Sulfanilamide Therapy, Proc. Soc. Exper. Biol. & Med. **38**: 479 (May) 1938.

8. King, F. H., and Leslie, Alan: Oxygen Saturation of Arterial Blood in the Cyanosis from Sulfanilamide, J. A. M. A. **110**: 2069 (June 18) 1938.

sulfanilamide does not materially reduce arterial oxygen saturation before it can be recommended as a therapeutic agent.

Gastrointestinal Manifestations.—Anorexia and nausea were frequent but seldom severe enough to interfere with the oral administration of the drug.

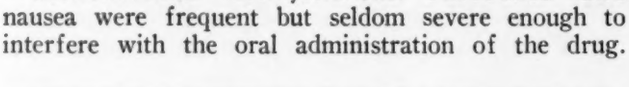

Chart 5.—Temperature in case 5.

TABLE 8 (case 5).—*Recovery from Type V Pneumonia and Bacteremia Following the Use of Sulfanilamide*

Patient a Negro aged 22; onset and admission May 20 and discharge June 2, 1938.

Day of Disease	Sulfanilamide, Dose in Grains	Blood Level in Mg. per 100 Cc.	Blood Picture				Blood Culture	Agglutination	Miscellany
			Hb.	R.B.C.	W.B.C.	NF-F%			
3	0	....	....	....	.....	.....	V	..	
4	160	....	13.0	4.97	21,400	73-13	V	..	X-ray, dense consolidation R.U.L.
5	120	10.1	13.0	....	16,600	68-15	Neg.	..	
6	120	9.0	13.5	5.2	17,500	52-20	Neg.	..	
7	120	10.0	12.0	4.22	13,100	51-30	.....	..	
8	60	9.8	13.5	....	13,100	64-19	.....	..	
9	0	....	....	....	.....	.....	.....	1:20	
12	0	....	13.0	5.32	.....	.....	.....	..	X-ray, resolution nearly complete

Vomiting and diarrhea were rare. Jaundice was present in the six patients in whom hemolytic anemia developed. In one other (chart 2 and table 4) toxic hepatitis developed. Since there was a coincidental extension of the pneumonia, the hepatitis may have been due to the pneumococcic infection.

Cerebral Manifestations.—Lassitude, headache and drowsiness were common toxic manifestations. Delirium developed in fourteen patients treated with sulfanilamide. With nine of these a history of chronic alcoholism was elicited and the clinical picture was typical of delirium tremens. With the other five it could not be definitely determined whether sulfanilamide or the pneumonia itself was responsible for the delirium.

Fever and Rash.—While it was frequently difficult to distinguish between fever due to sulfanilamide and that due to the disease itself, there were seven instances in which the fever continued in spite of apparent clinical improvement. In these cases the temperature tended to reach a peak in the early morning and fell in the afternoon. The fever subsided in all seven cases soon after administration of the drug was stopped. In two of the cases a morbilliform rash accompanied the fever.

Anemia.—In six of the patients treated with sulfanilamide acute hemolytic anemia developed, an incidence of 5.2 per cent. The total fall in hemoglobin content exceeded 4 Gm. per hundred cubic centimeters and the total fall in red cells was in excess of 1,500,000 per cubic millimeter in each case. The anemia developed abruptly in every case, appearing on the second day of sulfanilamide therapy in one case, on the third day in four and on the fifth day in one. In every case the hemoglobin content and red cell count continued to fall for two to three days after the drug therapy was discontinued. One patient had pneumococcic meningitis ten days after the onset of the anemia and died. The other five patients made a complete recovery with the aid of blood transfusions. Four returned for check counts some time after discharge. In one there was no appreciable change in the blood picture two months afterward. In the other three the check blood count was normal.

An example of acute hemolytic anemia developing after 170 grains (11 Gm.) of sulfanilamide is given in chart 6 and table 9 (case 6). The patient had type XIV pneumonia with bacteremia and leukopenia and was considered moribund at the time use of the drug was started. Within two days marked leukocytosis developed and the blood culture become sterile. A complete recovery eventually occurred. A similar abrupt neutrophilic leukocytosis accompanied the hemolytic anemia in four of the five remaining cases. This may prove a valuable warning sign.

In twenty-one additional cases (18.2 per cent) a more gradual and moderate fall in the hemoglobin content (between 2 and 4 Gm. per hundred cubic centimeters), with a comparable fall in the number of red cells (between 500,000 and 1,500,000 per cubic millimeter) occurred. In twelve of these the anemia appeared during the administration of sulfanilamide, and in the other nine it developed after the drug therapy was discontinued. Nine of the twenty-one patients had check blood

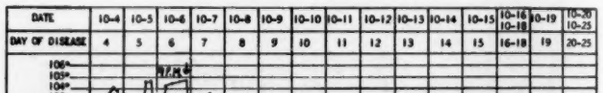

Chart 6.—Temperature in case 6.

TABLE 9 (case 6).—*Acute Hemolytic Anemia Following the Use of Sulfanilamide*

Patient a Negro woman aged 31; onset September 30, admission October 4 and discharge Oct. 25, 1937; tertiary syphilis.

Day of Disease	Oral Dose Sulfanilamide, Grains	Blood Level in Mg. per 100 Cc.	Blood Picture				Blood Culture	Miscellany
			Hb.	R.B.C.	W.B.C.	NF-F%		
4	..	...	....	....	5,700	20-56	.....	X-ray, consolidation R.U.L.
5	..	...	....	....	.....	.....	XIV	Sputum, type XIV
6	90	...	10.6	4.00	5,700	81-15	.....	Very toxic cyanotic, delirious
7	80	7.3	....	....	.....	.....	.....	X-ray, consolidation right lung
8	..	7.5	8.4	....	48,000	64-32	Neg.	Icteric index 50, much less toxic
9	..	...	3.8	....	32,000	55-33	.....	Pulse 150-160, transfusion 600 cc.
10	..	...	8.4	....	29,400	61-34	.....	
11	..	...	7.2	2.58	32,400	50-35	.....	Clinical evidence of resolution
12	..	...	5.6	2.85	29,600	69-24	.....	
13	..	...	5.6	2.35	19,400	49-40	.....	Transfusion, 500 cc.
15	..	...	7.4	2.60	8,100	21-48	.....	X-ray, resolution nearly complete; icteric index 6
19	..	...	9.4	3.30	.....	.....	.....	
20	..	...	....	....	.....	.....	.....	Clinical recovery

counts some time after discharge. One, who returned in two weeks, showed no change whereas the other eight, who returned after longer intervals, showed a satisfactory response. Thirty of the sulfanilamide group in whom anemia did not develop while they were in the hospital also returned for check blood counts after discharge. In every instance the blood count was as high as or higher than at discharge.

Acute hemolytic anemia was not observed among the control patients or serum-treated patients. Moderate secondary anemia developed in 11.6 per cent of such patients for whom adequate hematologic records were kept.

Leukocytosis—In none of the patients treated with sulfanilamide did granulocytopenia develop. In all four of the patients with an initial white cell count below 7,000 leukocytosis developed during sulfanilamide therapy, whereas six of the twelve whose initial count was between 7,000 and 10,000 showed a distinct rise after the drug therapy was started. The leukocytosis may have been due either to the infection or to liver extract, which was administered simultaneously to some of the patients, rather than to sulfanilamide. The abrupt leukocytosis which accompanied hemolytic anemia, however, was probably due to sulfanilamide.

COMMENT

While the results with sulfanilamide are encouraging, its place in the treatment of pneumonia has not been definitely determined. The future trend will probably be toward a combination of serotherapy and chemotherapy, particularly with types II and III. Osgood [9] found that a combination of sulfanilamide and serum was more effective against pneumococci in human bone marrow cultures than either preparation alone. We have used the two simultaneously in two cases of type I, in one case of type V and in two cases of type VII pneumonia without a fatality and in five cases of type II with one death.

Concerted efforts are being made to prepare derivatives that are more effective than sulfanilamide against the pneumococcus. Whitby [10] recently reported that sulfapyridine (2-[p-aminobenzene-sulfonamido] pyridine) will protect against minimum lethal doses of 10,000 pneumococci of types I, VII and VIII and against slightly smaller numbers of pneumococci of types II, III and V. Evans and Gaisford [11] reported a mortality rate of 8 per cent for 100 patients treated with this drug as compared with 27 per cent for 100 controls. Their results are unconvincing, however, since they are not analyzed from the standpoint of type, duration before treatment, extent of consolidation and incidence of bacteremia. Good results have been obtained in the laboratory with various sulfones.[12]

SUMMARY

This preliminary report is based on 115 cases of pneumococcic pneumonia treated with uniform doses of sulfanilamide and alternated with forty cases treated with Felton serum and ninety-four controls who received no specific therapy. The results were analyzed from the standpoint of the type of pneumococcus, average age of the patients, duration of the pneumonia before treatment, extent of the consolidation, blood culture, initial white cell count, duration after the onset of treatment, associated diseases and complications. The mortality rate was 15.7 per cent for the entire sulfanilamide group and 30.8 per cent for the controls. The death rate for fifty-seven patients with types I, II, V, VII and VIII pneumonia treated with sulfanilamide was 10.5 per cent, whereas it was 27.5 per cent for forty patients with the same types treated with serum. Of twenty-one patients with pneumococcic bacteremia treated with sulfanilamide seven died, of twelve treated with serum six died and of fifteen controls thirteen died. The most important toxic manifestation was anemia. In 5.2 per cent of the patients treated with sulfanilamide a severe hemolytic anemia developed and in an additional 18.2 per cent moderate secondary anemia developed.

9. Osgood, E. E.: A Comparative Study of the Effects of Sulfanilamide and Antipneumococcus Serum on the Course of Experimental Pneumococcic Infections, Arch. Int. Med. **62**: 181 (Aug.) 1938.

10. Whitby, L. E. H.: Chemotherapy of Pneumococcal Infections with 2-(P-Aminobenzenesulfonamido) Pyridine, Lancet **1**: 1210 (May 28) 1938.

11. Evans, G. M., and Gaisford, W. F.: Treatment of Pneumonia with 2-(P-Aminobenzenesulfamido) Pyridine, Lancet **2**: 14 (July 2) 1938.

12. Fourneau, Ernest; Trefouel, Jacques, M., and Mme.; Nitti, Frederico, and Bovet, Daniel: Chimiothérapie de l'infection pneumococcique par la di-(p-acétylaminophényl)-sulfone (1399F.), Compt. rend. Acad. d. sc. **205**: 299 (July 26) 1937. Bauer, Hugo, and Rosenthal, S. M.: Studies in Chemotherapy: Some New Sulfur Compounds Active Against Bacterial Infections, Pub. Health Rep. **53**: 40 (June 14) 1938.

PNEUMOCOCCIC PNEUMONIAS COMPLICATING PREGNANCY AND THE PUERPERIUM

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It has long been recognized that pneumonia is a serious complication of pregnancy with a considerably higher death rate than for nonpregnant women.[1] Some of the factors pertaining to pregnancy have received limited attention in the past,[2] but data concerning the pneumonias are scarce. From the practical possibilities of reducing mortality, recent developments in the fields of specific serum therapy and of chemotherapy have focused attention on the etiologic agents in infectious diseases, and this has been true particularly in the case of the pneumonias. References to the bacterial incitants of the pneumonias of pregnancy are very scarce and, until the recent reports of Bullowa [3] and of Rogers and Gooch,[4] have been limited to individual case reports.

There is at present a widespread interest among physicians and public health workers in the control of the mortality from pneumonia. Much of this attention is focused on etiologic diagnosis, particularly pneumococcus typing, and on the specific serum treatment of some of the pneumococcic pneumonias. It is appropriate therefore to present a series of 212 cases of "typed" pneumococcic pneumonia complicating preg-

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Owing to lack of space this article has been abbreviated for publication in THE JOURNAL by the omission of tables 1, 3, 4, 7, 10 and 11. The complete article appears in the authors' reprints.

Dr. Alexander W. Winkler assisted in the collection of the data in the earlier part of this study, and Dr. John W. Brown assisted with the more recent cases. Dr. Frederick C. Irving gave us permission to use the data from the Boston Lying-in Hospital, and Dr. K. Jefferson Thompson, former research fellow in obstetrics, carried out the serum treatment of a number of the patients there. The members of the staff of the obstetrics service of the Boston City Hospital cooperated.

1. Ramsdell, R. C.: Pneumonia in Pregnancy, Am. Med. **9**: 237-239 (Feb. 11) 1905. Jürgensen, T. H.: Croupous Pneumonia, in Ziemssen, Hugo: Cyclopedia of the Practice of Medicine, New York, W. Wood & Co., 1875, vol. 5, p. 25.

2. Wessinger, J. A.: Pneumonia Complicating Pregnancy, Am. Med. **12**: 213-216 (July) 1906. Ramsdell.[1] Jürgensen.[1]

3. Bullowa, J. G. M.: The Management of the Pneumonias, New York, Oxford University Press, 1937, pp. 439-443.

4. Rogers, E. S., and Gooch, M. E.: Type I Pneumococcus Pneumonia: Observations from a Study of Two Thousand Cases Treated with Specific Serum, New York State J. Med. **38**: 1369-1375 (Nov.) 1938.

nancy and the puerperium from the Boston City Hospital and the Boston Lying-in Hospital. The chief interest in this study concerns the classification of these cases according to the type of the pneumococcus and the influence of specific serum treatment on the mortality of the pneumonias due to some of these types. However, the effect on mortality of some of the other important factors concerning both the pneumonia and the pregnancy will be considered.

Only those patients have been included who had definite symptoms and physical and/or x-ray signs of pneumonia and from whose sputum, lung or pleural fluid or blood cultures pneumococci were identified and typed before July 1, 1938. About one third of the cases occurred before 1929, when typing was carried out only for types I, II and III. In almost all the remaining cases the pneumococci were classified with the aid of serums for the higher types.[5] Most of the serum treated patients received concentrated antipneumococcus horse serums. A few of the cases of type I pneumonia occurred between 1919 and 1922 and the patients were treated with unconcentrated type I antipneumococcus horse serum,[6] and in some of the recent cases homologous type-specific concentrated rabbit serums were given.[7] Five patients were treated nonspecifically with serums containing no antibodies for the homologous type of pneumococcus. These have been included among the non-serum treated patients. The pneumococcus typings were carried out by standard methods.[8] The Neufeld method[9] applied directly to sputum or to the peritoneal exudate of mice inoculated with sputum has been relied on for most of the rapid typing in the recent cases. At the Boston City Hospital, most of the prepartum pneumonia was treated in the medical services with the cooperation of the obstetrics staff. The postpartum pneumonias and those occurring late in pregnancy were usually treated in the obstetrics service with the cooperation of the staff of the medical services. Thirty of the cases are from the Boston Lying-in Hospital.

TABLE 2.—*Pneumococic Pneumonias Complicating Pregnancy and the Puerperium; Character of the Pulmonary Lesion in Relation to Delivery and Maternal Mortality*

	Lobar Pneumonia				Atypical Pneumonia*			
	Number of Patients	Number Died	Percentage Died	Percentage Bacteremic	Number of Patients	Number Died	Percentage Died	Percentage Bacteremic
Prepartum pneumonia...	106	30	28	36	36	17	47	39
Postpartum pneumonia...	38	7	18	40	32	13	41	17
All cases...	144	37	26	37	68	30	44	28

* Including patients with lobar pneumonia in some other parts of the lung.

5. Cooper, Georgia; Edwards, Marguerite and Rosenstein, Carolyn: The Separation of Types Among the Pneumococci Hitherto Called Group IV and the Development of Therapeutic Antiserums for These Types, J. Exper. Med. **49**: 461 (March) 1929. Cooper, Georgia; Rosenstein, Carolyn; Walter, Annabel, and Peizer, Lenore: The Further Separation of Types Among the Pneumococci Hitherto Included in Group IV and the Development of Antisera for These Types, ibid. **55**: 531 (April) 1932.

6. Locke, E. A.: The Treatment of Type I Pneumococcus Lobar Pneumonia with Specific Serum, J. A. M. A. **80**: 1507-1511 (May 26) 1923.

7. Finland, Maxwell, and Brown, J. W.: Specific Treatment of Pneumococcus Type I Pneumonia, Am. J. M. Sc. **197**: 151-168 (Feb.) 1939; Specific Treatment of Pneumococcus Type II Pneumonia, ibid., to be published; Specific Treatment of Pneumococcus Type V and Type VII Pneumonias, ibid., to be published.

8. Avery, O. T.; Chickering, H. T.; Cole, R. I., and Dochez, A. R.: Acute Lobar Pneumonia, Monograph 7, Rockefeller Institute for Medical Research, 1917. Sabin, A. B.: Microscopic Agglutination Test in Pneumonia, J. Infect. Dis. **46**: 469 (June) 1930.

9. Sabin, A. B.: Immediate Pneumococcus Typing Directly from the Sputum by the Neufeld Reaction, J. A. M. A. **100**: 1584 (May 20) 1933.

INCIDENCE

Since bacteriologic studies of cases of pneumonia have been made as a routine in very few clinics, the available figures concern all the pneumonias irrespective of cause and there are scant reliable data concerning the incidence of pneumococcic pneumonias associated with pregnancy. Norris and Farley[10] collected 13,611 cases of pregnancy, among which pneumonia was diagnosed in 120, or 0.8 per cent. Jürgensen[1] reported pneumonia among 2.3 per cent of 1,842 pregnant women. Wessinger[2] quoted figures from Vienna indicating that forty-seven, or 1.9 per cent, of 2,475 women with pneumonia were pregnant. Nuckels and Hertig[11] found twenty-three women with pneumococcic infections (probably all had pneumonia) among 20,364 delivered at the Boston Lying-in Hospital, an incidence of one case to 855 deliveries. They stated the general belief that pneumococcic infections are less common in pregnant than in nonpregnant women because of the comparatively sheltered existence of the former. Rogers and Gooch,[4] on the other hand, found the pregnancy rate (where the duration of pregnancy is six months or more) to be 6.6 per cent for their serum treated women of child-bearing age with type I pneumonia, as compared to an estimated 2.1 per cent rate of pregnancy in a similar age group in the general female population.

The data concerning the incidence of pneumonia at the Boston City Hospital for the arbitrarily chosen period 1931-1937, inclusive, were reviewed (table 1). All patients admitted during pregnancy or the puerperium and all those for whom a diagnosis of pneumonia was made irrespective of cause were included. Among the 13,446 patients with pneumonia, 1,277, or 9.5 per cent, were between 18 and 45 years of age. These included 164 pregnant or recently parturient women, constituting 1.2 per cent of all those with pneumonia, or 12.8 per cent of the women with pneumonia who were between 18 and 45 years of age. Among the 25,891 patients admitted to the hospital in the same period during pregnancy or the puerperium, the incidence of all pneumonias was 0.63 per cent, or one case of pneumonia in 158 cases. It is interesting to note that while lobar pneumonia was more frequent than the atypical pneumonias (bronchopneumonias) in all women between 18 and 45 (12.4 and 7.5 per cent respectively) the reverse was true of the pneumonias complicating pregnancy. With women of this age group, 10.4 per cent of the cases of lobar pneumonia occurred in association with pregnancy, as compared with 15.7 per cent of the cases of bronchopneumonia. This is consistent with previous observations to the effect that lobar pneumonia is usually a primary disease and that the atypical pneumonias are more often secondary to other serious conditions except in infants and in aged persons.[12]

CHARACTER OF THE PULMONARY LESIONS

Other features bearing on the character of the pulmonary lesions were brought out in an analysis of the cases of pneumococcic pneumonia under consideration, in 142 of which the condition occurred during preg-

10. Norris, G. W., and Farley, D. L., in Osler, William and McCrae, Thomas: Modern Medicine, Philadelphia, Lea & Febiger, 1913, vol. 1, p. 264.

11. Nuckels, H. H., and Hertig, A. T.: Pneumococcus Infections of the Genital Tract in Women, Especially During Pregnancy and the Puerperium, Am. J. Obst. & Gynec. **35**: 782 (May) 1938.

12. Finland, Maxwell: The Significance of Specific Pneumococcus Types in Disease, Including Types IV to XXXII (Cooper), Ann. Int. Med. **10**: 1531 (April) 1937.

nancy and in seventy of which it began after delivery. In approximately one in every four cases of pneumonia occurring during pregnancy the pneumonia was "atypical" or bronchopneumonia, whereas in about one half of the cases of pneumonia observed post partum the condition was atypical. The mortality for the atypical pneumonias was higher in each instance, in spite of a lower incidence of bacteremia (table 2). This, again, is in accord with the observations previously recorded for all pneumococcic pneumonias.[12]

TYPES OF PNEUMOCOCCI

The incidence of the various types among the 212 cases of pneumococcic pneumonia complicating pregnancy and the puerperium was similar to that found among 2,484 cases previously reported from the Boston City Hospital[12] (table 3). Type I was the most frequent type and accounted for about one fourth of the cases in each series. Among the other common types, types V and XIV had a somewhat higher incidence, type VII had the same incidence, and types II, III and VIII were somewhat less frequent in the cases of pneumonia complicating pregnancy. Since the mortality for the pneumonias caused by some of these types of pneumococci has been favorably influenced by treatment with type-specific antiserums[13] it is of interest to note the results in the cases of pneumonia complicating pregnancy.

MORTALITY AND BACTEREMIC INCIDENCE

It is necessary first to consider the general mortality in the present cases in comparison with all cases of pneumococcic pneumonia. Since age and bacteremia are the two most important factors influencing mortality, their effect was analyzed. In each decade the death rate was found to be higher for pneumonia complicating pregnancy and the puerperium than for all the pneumonias. This higher death rate was constantly associated with a higher incidence of bacteremia (table 4).

EFFECT OF SPECIFIC SERUM TREATMENT ON MORTALITY

Serum treatment for types other than I and II was available during the last three years of the study and was used mostly for pneumonia due to types V and VII pneumococci. The mortality rates for the serum treated and non-serum treated patients are listed by type in table 5. The death rate for all the fifty-four patients treated with specific serum was 20 per cent, as compared with 35 per cent for those who did not receive specific serum. These figures do not convey the complete picture, however, even when the bacteremic incidence is taken into account, for it is necessary to consider the various factors contributing to the death in each of the fatal cases. Some of these factors in most of the cases from the Boston City Hospital have been noted in previous reports concerning serum therapy[14] and need not be reviewed here in detail. Briefly, in almost every one of the patients who died after specific treatment, one or more of the following conditions contributed to the failure of serum therapy: (1) delayed treatment, that is, treatment begun after the fifth day of the pneumonia, (2) grossly inadequate amounts of specific antibody, (3) treatment undertaken when the patient was in poor general condition, death occurring within a few hours, (4) mixed infections, notably hemolytic streptococcus sepsis, (5) focal complications, including vegetative endocarditis and (6) general systemic complications, such as decompensated heart disease or eclampsia.

It is of interest that Rogers and Gooch[4] had the same death rate, 19 per cent, for their forty-two serum treated pregnant patients with type I pneumonia, as compared with 11 per cent for serum treated nonpregnant patients aged from 15 to 45 with type I pneumonia. Bullowa's[3] nineteen serum treated pregnant patients with type I pneumonia included six with bacteremia. There were five deaths, all associated with bacteremia. His entire series included fifty-nine patients with pneumococcic pneumonia complicating pregnancy; twenty-nine were serum treated, with ten deaths (34 per cent), and thirty were not serum treated, with seven deaths (23 per cent). However, there were seven bacteremic patients among the ten serum treated patients who died and only two among the seven non-serum treated patients, indicating that the patients with severest involvement were chosen for treatment with serum. In Ramsdell's[1] 352 collected cases of pneumonia in pregnancy (without respect to cause), there were ninety-six deaths, or 27.3 per cent, as compared with a general mortality for pneumonia of 20 per cent.

TABLE 5.—*Pneumococcic Pneumonias Complicating Pregnancy and the Puerperium; Death Rates in Relation to Bacteremia and to Specific Serum Treatment*

		Blood Culture									
		Positive		Negative		Not Done		All Patients			
Type	Specific Treatment	Number of Patients	Number Died	Number of Patients	Number Died	Number of Patients	Number Died	Number of Patients	Number Died	Percentage Died	Percentage Bacteremic
I	Serum	14	2	15	2	3	2	32	6	19	48
	No serum	9	5	8	0	6	2	23	7	30	53
II	Serum	5	1	2	0	0	..	7	1	14	71
	No serum	0	..	3	0	4	1	7	1	14	0
V	Serum	3	1	5	2	0	..	8	3	38	38
	No serum	7	5	3	2	2	2	12	9	75	70
VII	Serum	1	0	3	0	1	0	5	0	0	25
	No serum	1	1	3	0	2	0	6	1	17	25
All types	Serum	23	4	27†	5	4	2	54	11	20	46
	No serum*	28	21	70	16	60	19	158	56	35	29

* Including patients treated with heterologous serums.
† Including one patient with type XIV pneumonia who died and one with type IX who recovered

COMPLICATIONS

Focal purulent complications were frequent among these patients, as may be expected from the high incidence of bacteremia.[15] They occurred in both the serum treated and the non-serum treated patients. Only the more common ones need be mentioned.

Empyema was the most frequent and occurred in ten serum treated and in fourteen non-serum treated patients; four of the former and eight of the latter died. This complication occurred predominantly with type I pneumonia, eight of the serum treated and five of the non-serum treated patients with empyema having

13. Bullowa,[3] Finland and Brown.[7]

14. Sutliff, W. D., and Finland, Maxwell: Type I Pneumococcic Infections with Especial Reference to Specific Serum Treatment, New England J. Med. **210**: 237-245 (Feb. 1) 1934; The Specific Serum Treatment of Pneumococcus Type II Pneumonia, J. A. M. A. **100**: 560-566 (Feb. 25) 1933. Finland, Maxwell, and Tilghman, R. C.: Clinical and Immunologic Observations in Cases of Pneumococcus Type V Pneumonia Treated with Specific Antibody, New England J. Med. **215**: 1211-1221 (Dec. 24) 1936. Finland and Brown,[7] Finland, Maxwell; Tilghman, R. C.; Ruegsegger, J. M., and Dowling, H. F.: Clinical and Immunological Observations in Cases of Pneumococcus Type VII Pneumonia Treated with Concentrated Type-Specific Antibody, Am. J. M. Sc. **193**: 59 (Jan.) 1937.

15. Tilghman, R. C., and Finland, Maxwell: Clinical Significance of Bacteremia in Pneumococcic Pneumonia, Arch. Int. Med. **59**: 602-619 (April) 1937.

this type. Subcutaneous pneumococcic abscess occurred in five of the bacteremic patients who recovered; three were serum treated and two were not. Pneumococcic otitis media occurred in one serum treated and in three non-serum treated patients who recovered. Hemolytic streptococcus sepsis, including pleural and puerperal infections, occurred in four of the serum treated and in seven of the non-serum treated patients, and only one of the latter recovered. Endometritis with pneumococci cultured from the uterus or lochia occurred in the following five cases: a fatal case of non-serum treated type I pneumonia with bacteremia following a forceps delivery; a case of serum treated type II pneumonia with bacteremia following normal delivery, with subcutaneous pneumococcic abscesses in addition, with recovery; a fatal case of non-serum treated type I pneumonia following cesarean section; a case of non-serum treated type XXIII pneumonia following cesarean section, and a fatal case of non-serum treated type II pneumonia following a septic induced abortion. In addition, three non-serum treated patients had pneumococcic peritonitis limited mostly to the pelvis; these included

TABLE 6.—*Mortality of Pneumococcic Pneumonia in Relation to Duration of Pregnancy*

	Number of Patients	Died	Percentage Died
First trimester	20	6	30
Second trimester	54	12	22
Before seventh month	74	18	24
Third trimester	51	24	47
At term	17	5	30
Seventh month and later	68	29	43
Post partum	70	20	29
Pre partum: serum	38	8	21
no serum	104	39	38
Post partum: serum	16	3	19
no serum	54	17	31

one patient with type II, one with type III and one with type V pneumonia. In all cases the pneumonia followed an induced abortion. The patient with type III survived, and the other two patients died. One of the non-serum treated patients with type VIII died with meningitis, and a serum treated patient with type V died with rheumatic heart disease and vegetative endocarditis. Lung abscesses occurred in four non-serum treated patients, two of whom died.

EFFECT OF THE DURATION OF PREGNANCY ON MATERNAL MORTALITY

Death rates have usually been found to be higher for pneumonia occurring in the late months of pregnancy than for pneumonia occurring in the earlier months. In Ramsdell's [1] cases there were thirty-two deaths (22 per cent) among 144 cases of pneumonia occurring in the first six months of pregnancy, as compared with fifty deaths (30.5 per cent) among the 164 cases of pneumonia occurring after the sixth month. Harris [16] found a steadily increasing mortality up to 61 per cent in the last month of pregnancy for his collected cases of influenza with pneumonia. Among Rogers and Gooch's [4] serum treated patients with type I there was one death among fourteen women less than six months pregnant (7.1 per cent), as compared with seven deaths among twenty-seven women who had been pregnant six months or longer (25.9 per cent). In the present series there are almost equal numbers of cases of postpartum pneumonia, cases of pneumonia complicating pregnancy of six months' duration or less and cases of pneumonia complicating pregnancy of more than six months' duration. The death rates in each of these groups are listed in table 6. The highest death rate was for the women in the third trimester of pregnancy. The cases of pneumonia occurring at term or post partum have a somewhat lower mortality. The serum treated patients had an appreciably lower death rate than the non-serum treated patients. This was true for both the cases of prepartum and the cases of postpartum pneumonia. This will be referred to again in relation to the interruption of pregnancy.

PARITY AND MATERNAL MORTALITY

There were twelve deaths among forty-five primiparas (27 per cent) and fifty-three deaths among 165 multiparas (37 per cent). With the non-serum treated patients the death rate was appreciably lower for the primiparas than for the multiparas (26 and 38 per cent respectively). The death rate for forty-eight multiparous serum treated patients was 19 per cent, in contrast with a 38 per cent mortality for 117 similar non-serum treated patients. There were two deaths among the six primiparous serum treated patients, but one of these deaths was associated with eclampsia and the other with rheumatic heart disease and vegetative endocarditis. In Ramsdell's [1] series there were eight deaths among eighty-nine multiparas (20 per cent) and four deaths among thirteen primiparas (31 per cent). The effect of age in the present series has already been noted (table 4). In Ramsdell's cases the death rate for patients under 25 was 13.3 per cent, for those from 25 to 35 it was 23.3 per cent and for those over 35 it was 22 per cent.

TERMINATION OF PREGNANCY DURING THE PNEUMONIA

Pregnancy was terminated in more than one half of all the cases (55 per cent) (table 8). It was terminated more frequently in the fatal cases than in those of recovery, 70 per cent of the patients who died and 48 per cent of those who recovered aborting in the course of the infection. Likewise, abortion was less frequent in the first six months of pregnancy (43 per cent) than after the sixth month (69 per cent). However, the lower incidence of abortions before the sixth month was limited to the cases of recovery. The pregnancy was terminated in about one third of the women who were pregnant six months or less and recovered, whereas about two thirds of all the other patients were delivered. The frequency of delivery was similar for the serum treated and the non-serum treated patients (table 9). In Ramsdell's cases 52 per cent of those in the first six months aborted, as compared with 70 per cent of those pregnant more than six months. Of his patients who died, 85.4 per cent were delivered.

EFFECT OF DELIVERY ON MATERNAL MORTALITY

In Ramsdell's cases there were seventy deaths among 190 patients with pneumonia who aborted, or 36.7 per cent, as compared with twelve deaths, or 10.7 per cent, among 118 patients who did not abort. In Harris's [16] cases of influenza with pneumonia complicating pregnancy, there were 41 per cent of deaths among 383 cases in which pregnancy was uninterrupted as compared with 63 per cent of deaths among 395 cases in which pregnancy was ended. In the present series (table 9) the lower death rate was limited to the women who were pregnant less than six months and were not delivered. None of the nine serum treated patients in

16. Harris, J. W.: Influenza Occurring in Pregnant Women, J. A. M. A. **72**: 978-980 (April 5) 1919.

this group died, and five, or 15 per cent, of the thirty-two non-serum treated patients died. For all the patients delivered and for those who were more than six months pregnant and were not delivered, the death rate was between 45 and 50 per cent without serum therapy and between 25 and 30 per cent with such therapy. The combined death rate for serum treated and non-serum treated patients was 22 per cent for the undelivered patients and 42 per cent for those who were delivered.

The termination of pregnancy took place at almost any time during the course of the pneumonia (table 10). About one half of the patients were delivered during the first five days of the disease. Among the forty-one patients delivered during the first five days of the pneumonia, nineteen, or 46 per cent, died, as compared with fourteen, or 39 per cent, among the thirty-six patients delivered after the fourth day. In Ramsdell's series 40 per cent of those who aborted before the third day died, as compared with 28 per cent of the sixty-nine who aborted after the third day.

RELATION OF SERUM TREATMENT, DELIVERY AND MATERNAL DEATHS

There were thirty-eight serum treated patients among those who had pneumonia before parturition. Of the sixteen who were not delivered, two died. Treatment with serum was begun before delivery with eleven patients, of whom two died, and serum was given to eight other patients after delivery and two of these patients died. In the three remaining cases, delivery took place on the day treatment was begun and two of the patients died after treatment.

DURATION OF THE PNEUMONIA

The number of days from the onset of the acute symptoms of pneumonia to death or to recovery by crisis or lysis was also analyzed (table 11). The numbers of cases are too few to indicate anything more than the trend. In the undelivered patients death

TABLE 8.—*Frequency of Delivery During Pneumococcic Pneumonia Complicating Pregnancy*

	Recovered			Died			All Patients		
Duration of Pregnancy	Number of Patients	Delivered	Percentage Delivered	Number of Patients	Delivered	Percentage Delivered	Number of Patients	Delivered	Percentage Delivered
First three months	14	5	36	6	5	83	20	10	50
Second three months	42	14	33	12	8	67	54	22	41
Six months or less	56	19	34	18	13	72	74	32	43
Third three months	27	17	65	24	17	71	51	34	67
At term	12	10	83	5	3	60	17	13	76
Seven months or more	39	27	69	29	20	69	68	47	69
Total	95	46	48	47	33	70	142	79	55

tended to occur early, that is between the third and the sixth day, in those who were pregnant more than six months and was delayed until the seventh day or later in those who were in the first two trimesters of pregnancy. In the patients who were delivered, death occurred a week or more after the onset in most of the cases, except for about one third of those in late pregnancy, who died on or before the sixth day. Of the patients who recovered, crisis tended to occur somewhat earlier in the undelivered ones. Thus about two thirds of the undelivered patients had a crisis within seven days, while only one third of the delivered patients reached the crisis by the end of the seventh day.

FATE OF THE FETUS

Among the seventy-nine patients with pneumococcic pneumonia who were delivered during pregnancy thirty-one (39 per cent) had living babies, thirteen (16 per cent) had babies who died soon after birth and thirty-five (44 per cent) had stillbirths. Of the thirty-one mothers who were delivered of living babies nine (29 per cent) died, whereas about one half of the remaining mothers died. The death rate was about the same for those with stillbirths and for those whose babies died

TABLE 9.—*Maternal Mortality of Prepartum Pneumococcic Pneumonias in Relation to the Fate of Pregnancy*

	Not Delivered			Delivered			
	Number of Patients	Number Died	Percentage Died	Number of Patients	Number Died	Percentage Died	Percentage Delivered
Sixth month or before							
Serum treated	9	0	0	10	3	30	53
Non-serum treated	33	5	15	22	10	46	40
Seventh month or later							
Serum treated	7	2	29	12	3	25	63
Non-serum treated	14	7	50	35	17	49	71
All patients with prepartum pneumonia							
Serum treated	16	2	13	22	6	27	58
Non-serum treated	47	12	26	57	27	47	55

soon after delivery. In almost all the cases the labor was very brief and in many it was followed by varying degrees of peripheral vascular collapse (shock).

As shown in table 12 there was no marked predominance of any particular type of delivery in the cases of postpartum pneumonia. In about one fourth of the cases the pneumonia occurred after cesarean section and in a similar number it followed abortion, either spontaneous or self induced. In the remaining cases the delivery was either entirely normal or some anesthesia (usually nitrous oxide, oxygen and ether) was used during a difficult labor or during the application of forceps. The maternal death rate was lowest for the women who were delivered spontaneously or who had a brief anesthesia during the application of forceps.

The fate of the fetus in the cases of postpartum pneumonia is also shown in table 12. In all the cases of abortion the abortion occurred before the seventh month, and only one of the sixteen babies lived for a short time after delivery. Of the fifty-four mothers who were delivered at term and later had pneumonia, forty-six had normal living babies and twelve (26 per cent) of the mothers died of the pneumonia. Four of the remaining eight mothers had stillbirths and the other four had babies who lived for a short time after delivery. One of the latter mothers died of her pneumonia.

TIME OF ONSET OF POSTPARTUM PNEUMONIA

In almost all of the cases of postpartum pneumonia the condition began within the first two weeks after delivery (table 13). In slightly more than one third of the cases, the pneumonia began on the second day post partum, and three fourths of all the patients had their initial symptom during the first three days post partum.

COMMENT

Pneumonia complicating pregnancy has a double interest. It concerns the obstetrician because of the high maternal and fetal mortality which it entails, and it concerns the internist because it carries with it a considerably higher death rate than pneumonia in nonpregnant women. It accounts for about one death in every

5,000 deliveries [17] and is the cause of about one half of the maternal deaths that are due to nonobstetric causes.[18] There can be little doubt that pneumonia complicating pregnancy warrants every possible consideration in an attempt to curtail the death rate. Now that effective specific serums are available for the large majority of the pneumococcic pneumonias, it is important to use the diagnostic procedures necessary for identification of the etiologic agent and to type the pneumococci as soon as the diagnosis of pneumonia is suspected. Early and adequate treatment with the homologous type-specific antipneumococcus serums can be expected to reduce materially the high death rate from the pneumonias when they complicate pregnancy, as demonstrated in the cases presented.

The dosage of serum in the treatment of pneumococcic pneumonia has been considered elsewhere.[7] The higher death rate and particularly the higher incidence of bacteremia in the cases of pneumonia complicating pregnancy are definite indications for larger doses than of severe pneumococcic pneumonias, such as those considered here. Other derivatives, such as sulfapyridine, may prove to be very useful, but there are good reasons for the belief that the greatest benefits from these drugs in the treatment of pneumococcic pneumonias will be obtained from their use in conjunction with specific antipneumococcus serums. The pneumonias of pregnancy are sufficiently serious to warrant the use of every available means of treatment, and the proved efficacy of specific serum therapy warrants primary consideration in those cases in which it is applicable.

SUMMARY

Data were studied concerning the incidence of pneumonia in pregnancy at the Boston City Hospital. About one of every eight women of child-bearing age who had pneumonia was pregnant, 0.63 per cent of all women admitted during pregnancy or parturition had pneumonia and in 1.2 per cent of all the cases of pneumonia the condition was complicated by pregnancy.

TABLE 12.—*Pneumococcic Pneumonia Complicating Pregnancy and the Puerperium; Maternal Mortality in Relation to the Fate of the Fetus*

	Delivered Patients									Undelivered Patients		
	Living Baby		Stillborn		Baby Died After Delivery		Total Delivered					
	Number	Died	Number	Died	Number	Died	Number	died	Percentage Died	Number	Died	Percentage Died
Before seventh month	3	1	26	11	3	1	32	13	41	42	5	12
Seventh month or later	28	8	9	7	10	5	47	20	43	21	9	43
Total cases of prepartum pneumonia	31	9	35	18	13	6	79	33	42	63	14	22
Postpartum Pneumonia												
Normal spontaneous delivery	12	2	2	0	0	..	14	2	14			
Anesthesia only	10	4	0	..	0	..	10	4	40			
Instruments and anesthesia	11	1	0	..	2	0	13	1	8			
Cesarean section and anesthesia	13	5	2	0	2	1	17	6	35			
Spontaneous or induced abortion	..	..	15	5	1	0	16	5	31			
Total cases of postpartum pneumonia	46	12	19	5	5	1	70	20	29			

are used for nonpregnant patients. These larger doses have been recommended in the Massachusetts pneumonia control program [19] and were used in the present cases. As much as 1,400 cc. of unconcentrated type I serum was given in some of the earlier cases in this series. The average dose in the recent cases was more than 250,000 units, which is higher than that used in other patients of the same age groups.[7]

It is too soon to evaluate the place of chemotherapy in the treatment of pneumonia. There is no doubt that the use of sulfanilamide has materially reduced the death rate from hemolytic streptococcus infections, which are responsible for most puerperal sepsis. That this drug may favorably influence streptococcic pneumonia is to be anticipated, although there is no convincing evidence so far that it does. The drug is known to enter the fetal circulation and the mother's breast milk,[20] but its influence on the baby or the fetus has not yet been determined. There is no good evidence that sulfanilamide itself has curative value in the treatment

A series of 212 cases of typed pneumococcic pneumonia complicating pregnancy and the puerperium which occurred at the Boston City Hospital and the Boston Lying-in Hospital were analyzed with respect to the more important features concerning both the pneumonia and the pregnancy.

The incidence of pneumococcic types in these cases was similar to that found in all cases of pneumonia in adults. The types for which specific antipneumococcus serum has proved effective were the most frequent.

TABLE 13.—*Interval Between Delivery and Onset of Postpartum Pneumonia*

Days	1	2	3	4	5	6	7	8-15	16+	Total
Number of cases	15	24	12	2	4	1	2	6	2	68

Bacteremia was more frequent than in all cases for the same age groups and the death rates were higher than in corresponding cases for the same age group.

The death rates were highest for late pregnancy and for women whose pregnancy was terminated during the disease.

The death rate for all the serum treated patients was almost one half of that for the corresponding nonserum treated patients. The lower death rates were for pneumonia complicating both early and late pregnancy, for postpartum pneumonia, for women who were delivered and those whose pregnancy was unaffected.

The frequency with which pregnancy was terminated did not seem to be influenced by serum treatment.

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19. Lord, F. T., and Heffron, Roderick: Pneumonia and Serum Therapy, New York, the Commonwealth Fund, 1938.

20. Stewart, H. L., Jr., and Pratt, J. P.: Sulfanilamide Excretion in Human Breast Milk and the Effect on Breast-Fed Babies, J. A. M. A. **111**: 1455 (Oct. 15) 1938. Barker, R. H.: The Placental Transfer of Sulfanilamide, New England J. Med. **219**: 41 (July 14) 1938. Pinto, S. S.: The Excretion of Sulfanilamide and Acetylsulfanilamide in Human Milk, J. A. M. A. **111**: 1914 (Nov. 19) 1938. Speert, Harold: Passage of Sulfanilamide Through the Human Placenta, Bull. Johns Hopkins Hosp. **63**: 337 (Nov.) 1938.

THE TREATMENT OF PNEUMOCOCCIC MENINGITIS WITH SULFANILAMIDE

REVIEW OF THE LITERATURE AND REPORT OF SIX ADDITIONAL CASES

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In a review of the literature to the year 1927 the Goldsteins [1] collected 150 authentic recoveries from pneumococcic meningitis and there are listed in the *Quarterly Cumulative Index Medicus* approximately thirty additional recoveries during the years 1927 to 1937. Most of these favorable outcomes have been attributed to spinal drainage and the administration of antipneumococcus serum or ethylhydrocupreine (optochin), but in general results with these therapeutic measures have been unsuccessful.

In the ten years preceding 1937 there were in the Children's Hospital of Cincinnati and in the pediatric service of the Cincinnati General Hospital twenty-three children suffering from pneumococcic meningitis, the mortality in this group being 100 per cent. Since the use of sulfanilamide three patients with the condition have recovered of a total of six treated. The histories of these six patients are summarized.

In table 1 are listed thirty cases of recovery from pneumococcic meningitis in which the treatment consisted in part of the administration of sulfanilamide or related compounds.

In table 2 are listed the reports of eight cases of pneumococcic meningitis treated with sulfanilamide or related compounds in which death occurred.

From the Children's Hospital Research Foundation and the Department of Pediatrics, University of Cincinnati College of Medicine.

1. Goldstein, H. I., and Goldstein, H. Z.: Pneumococcus Meningitis and Endocarditis: Report of Twenty Cases of Pneumococcic Meningitis With and Without Pneumococcic Endocardtis; Consideration of Treatment and Review of Literature, Internat. Clin. **3**: 155-219 (Sept.) 1927.

REPORT OF CASES

CASE 1.—*Pneumococcic meningitis (type V) following otitis media and mastoiditis.* C. M., aged 9 years, had had otitis media with drainage from the right ear for five days and meningeal signs for twenty-four hours. Antimeningococcus serum was given intranspinally prior to admission. Cultures of material from the ears and of the spinal fluid were positive for pneumococcus type V and of material from the mastoid region were negative. Roentgenograms of the mastoid regions showed cloudiness of the cells on the right; at operation pus was found in the right mastoid region. Blood cultures on the first and second days were negative. Cultures of the spinal fluid were negative on the third day and thereafter. The clinical course was mild. The patient received a total of 27 Gm. of sulfanilamide by mouth and an equal amount of sodium bicarbonate; ethylhydrocupreine hydrochloride (2.7 Gm.) was also given. There were no toxic effects. Recovery was complete.

CASE 2.—*Pneumococcic meningitis (type III) following otitis media and mastoiditis.* A. M., aged 10 years, had had bilateral otitis media for one week and headache, drowsiness and stiffness of the neck for twelve hours. Cultures of material from the ears showed an intermediate type of streptococcus, of material from the mastoid region a hemolytic Streptococcus aureus and of the spinal fluid pneumococcus type III. Roentgenograms of the mastoid regions showed cloudiness of the cells on the left; at operation pus and sclerotic cells were found in the left mastoid region. Four blood cultures were negative. Cultures of the spinal fluid were negative on the fourth day and thereafter. The patient received a total of 24 Gm. of sulfanilamide and an equal amount of sodium bicarbonate by mouth and small amounts of 0.8 per cent sulfanilamide intraspinally and intravenously daily for seven days; ethylhydrocupreine hydrochloride (0.7 Gm.) was also given. There were no toxic effects. Recovery was complete.

CASE 3.—*Pneumococcic meningitis (type III) following otitis media and mastoiditis.* M. T., aged 8 years, had had bilateral otitis media one month before, but recovery was apparently complete. On admission the complaints were chill, frontal headache and photophobia. There was bilateral bulging of the ear drums. Cultures of material from the ears after myringotomy showed Staphylococcus aureus, of material from the mastoid regions an unidentified diphtheroid and of the spinal fluid pneumococcus type III. Roentgenograms of the mastoid regions showed slight clouding of the cells on both sides, more

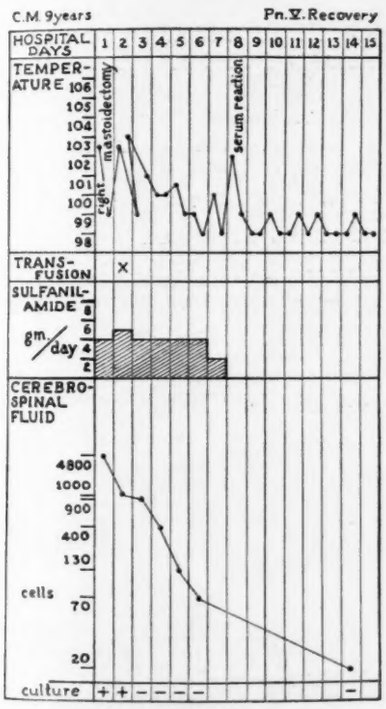

Chart 1.—Observations in case 1.

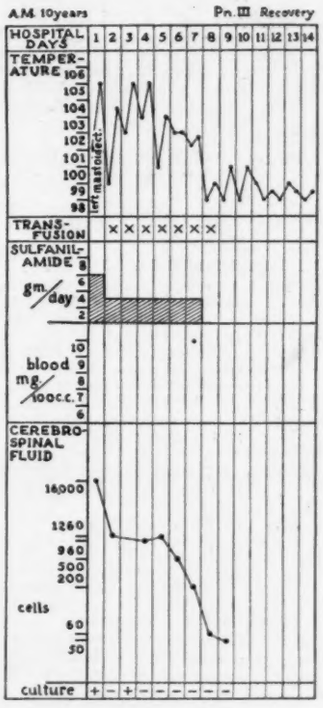

Chart 2.—Observations in case 2.

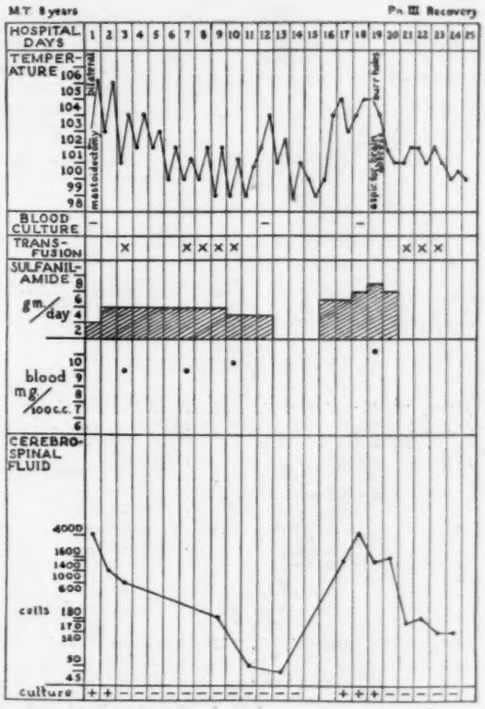

Chart 3.—Observations in case 3.

marked on the left; at operation pus was found in both mastoid regions. Blood cultures on the first, twelfth and eighteenth days were negative. Cultures of the spinal fluid were negative on the third day. Some clinical improvement was noted at this time. On the twelfth day slight dyspnea developed and the heart was markedly enlarged, as demonstrated by physical examination and roentgenogram. The patient became worse on the sixteenth and seventeenth days, when there was increased pressure of the spinal fluid and when also the spinal fluid cultures were again positive. There were no localizing signs of brain abscess until the eighteenth day, when a definite left homonymous hemianopia and weakness of the left arm and left leg were present. Trepanation was performed and burr holes made in the skull; 16 cc. of pus was aspirated from the right temporal region. Ventricular and lumbar punctures were performed every eight hours from the nineteenth to the twenty-first day. There was slow improvement. The patient received a total of 64 Gm. of sulfanilamide with an equal amount of sodium bicarbonate; ethylhydrocupreine hydrochloride (1.6 Gm.) was also given. Recovery was complete.

CASE 4.—*Pneumococcic meningitis (type III) following otitis media and mastoiditis.* W. L., aged 9 years, had had bilateral otitis media with a high fever for one week and swelling in front of the right ear for two days. Cultures of material from the ears showed Staphylococcus albus, from the right mastoid no growth and from the left mastoid a gram-positive spore-

TABLE 1.—*Recoveries from Pneumococcic Meningitis in Patients Treated with Sulfanilamide Compounds*

Reference	Age, Years	Probable Source of Infection	Type of Pneumococcus in Spinal Fluid	Treatment	Drug Approximate Total, Gm.	Free Sulfanilamide in Blood, Mg. per 100 Cc.	Comment
				PRONTOSIL			
Latto, C.: Brit. M. J. **1**: 566 (March 12) 1938	26	No focus? primary? blood culture not noted	I	3 lumbar punctures; large doses of prontosil, amounts not shown	Large amount	.....	Spinal fluid culture sterile twelfth day
Landon, J.: Brit. M. J. **1**: 844 (April 16) 1938	5	Infection of upper part of respiratory tract; blood culture not noted	..	2 lumbar punctures; prontosil intramuscularly, 80 cc. in 4 days	2.0	.....	Hematuria and purpuric rash developed
Caldwell, J. R., and Byrne, P. S.: Brit. M. J. **1**: 1204 (June 12) 1937	16	Sore throat; blood culture not noted	I	Prontosil by mouth and intramuscularly, amounts not shown	.....	.....	
				PRONTOSIL AND SULFANILAMIDE			
Mertins, P. S., and Mertins, P. S., Jr.: Arch. Otolaryng. **25**: 657 (June) 1937	13	Mastoiditis; blood culture negative	IV	Mastoidectomy; prontosil (2.5%), 40 cc. a day for 6 days; sulfanilamide by mouth, total 6 Gm. in 3 days	12.0	.....	
Neal, J. B., and Appelbaum, E.: Am. J. M. Sc. **195**: 175 (Feb.) 1938	..	After tonsillectomy and ethmoid sinus operation; blood culture not noted	XXXI	Prontosil and sulfanilamide by mouth, amounts not shown	.....	.....	
		After submucous resection and turbinate operation; blood culture not noted	XXIX	Prontosil and sulfanilamide, amounts not shown	.....	.....	
		Otitis media and mastoiditis; blood culture not noted	IV	Mastoidectomy; prontosil and sulfanilamide, amounts not shown	.....	.....	
				SULFANILAMIDE			
Basman, J., and Perley, A. M.: J. Pediat. **11**: 212 (Aug.) 1937	9	Otitis media and mastoiditis; blood culture negative	V	Antimeningococcus serum intraspinally once; transfusions; sulfanilamide intravenously, intramuscularly, intraspinally and subcutaneously, total 82 Gm. in 18 days; mastoidectomy 5 weeks after admission	82.0	4-11	Spinal fluid culture sterile ninth day
Allan, W. B.; Mayer, S., Jr., and Williams, R.: Am. J. M. Sc. **196**: 99 (July) 1938	16	Skull fracture through frontal and ethmoid sinuses; blood culture negative	XIV	Frequent lumbar punctures; sulfanilamide by mouth, total 35.6 Gm. in 8 days	35.6	5-7	Spinal fluid culture sterile second day
	42	Infection of upper part of respiratory tract; blood culture negative	XXIX	Sulfanilamide by mouth, total 46.5 Gm. in 10 days	46.5	8-10	Spinal fluid culture sterile second day; dramatic recovery
	13	Frontal sinusitis; blood culture negative	XX	Frequent lumbar punctures; radical frontal sinus operation; continuous spinal drainage; 4 transfusions; sulfanilamide by mouth, intraspinally and subcutaneously, total 35 Gm. in 5 days	35.0	5-10	Spinal fluid culture negative fourth day; anemia and jaundice developed
Finland, M.; Brown, J. W., and Rauh, A. E.: New England J. Med. **218**: 1033 (June 23) 1938	19	After removal of brain tumor; 3 negative blood cultures	XVII	Frequent lumbar punctures; transfusion; sulfanilamide by mouth, total 325 Gm. in 9 weeks	325.0	5-15	Spinal fluid culture sterile fifth week; anemia developed
Young, F.: Brit. M. J. **2**: 286 (Aug. 6) 1938	5	Otitis media; blood culture not noted	..	Antimeningococcus serum intraspinally once; sulfanilamide by mouth, total 10.5 Gm. in 4 days; with recurrence, 12.5 Gm. in 13 days; mastoidectomy not done	23.0	.....	Spinal fluid culture sterile seventh day
Gubner, J.: Arch. Otolaryng. **28**: 241 (Aug.) 1938	5½	10 days after mastoidectomy; blood culture not noted	III	Frequent lumbar punctures; exploration of mastoid wound; transfusions; sulfanilamide, total 75 Gm. in 26 days	75.0	6-14	Spinal fluid culture sterile thirteenth day
Tixier, L.; Eck, M., and Grossiard: Bull. Soc. pédiat. de Paris **36**: 118 (March) 1938	11	Primary? blood culture not noted	I	Frequent lumbar punctures; sulfanilamide by mouth, total 19 Gm. in 12 days	19.0	.....	Spinal fluid culture sterile third day; dramatic recovery
Hubert, C.: Rev. de laryng. **59**: 365 (April) 1938	17	Otitis media; blood culture not noted	III	Mastoidectomy; frequent lumbar punctures; sulfanilamide by mouth, total 100 Gm., 1 Gm. intraspinally (0.8% sulfanilamide) in 11 injections	101.0	.....	Spinal fluid culture sterile fourth day
Hewell and Mitchell case 1 (chart 1)	9	Otitis media and mastoiditis; blood culture negative	V	Mastoidectomy; frequent lumbar punctures; transfusions; sulfanilamide by mouth, total 27 Gm. in 7 days; ethylhydrocupreine 2.7 Gm.	27.0	.....	Spinal fluid culture sterile third day
Case 2 (chart 2)	10	Otitis media and mastoiditis; blood culture negative	III	Mastoidectomy; frequent lumbar punctures; sulfanilamide by mouth, intravenously and intraspinally, total 24 Gm. in 7 days; ethylhydrocupreine 0.7 Gm.	24.0	10	Spinal fluid culture sterile fourth day

TABLE 1.—*Recoveries from Pneumococcic Meningitis in Patients Treated with Sulfanilamide Compounds—Continued*

Reference	Age, Years	Probable Source of Infection	Type of Pneumococcus in Spinal Fluid	Treatment	Drug Approximate Total, Gm.	Free Sulfanilamide in Blood, Mg. per 100 Cc.	Comment
Case 3 (chart 3)	8	Otitis media and mastoiditis; blood culture negative	III	Mastoidectomy; operation for brain abscess; frequent lumbar punctures; sulfanilamide by mouth, total 64 Gm. in 17 days; ethylhydrocupreine 1.6 Gm.	64.0	8-12	Spinal fluid culture sterile third day
		SULFANILAMIDE + SPECIFIC ANTIPNEUMOCOCCUS SERUM + AUTOGENOUS SERUM					
Finland, Brown and Rauh	8	Fracture of skull; meningitis following débridement; 4 negative blood cultures	VII	Frequent lumbar punctures; sulfanilamide by mouth, total 70 Gm. in 20 days; specific antipneumococcus serum intravenously and intraspinally; autogenous serum intraspinally	70.0	10-12	Spinal fluid culture sterile fifth day
	7	Fracture of skull; 3 negative blood cultures	XIX	Transfusion; sulfanilamide by mouth, total 51 Gm. in 8 days; specific antipneumococcus serum intravenously; autogenous serum intraspinally	51.0	10-20	Spinal fluid culture sterile in 48 hours; anemia developed
	13	Infection of upper part of respiratory tract; 3 negative blood cultures	XXVIII	Sulfanilamide by mouth, total 106 Gm. in 14 days; specific antipneumococcus serum (rabbit) intravenously; autogenous serum and specific serum intraspinally	106.0	15	Spinal fluid culture sterile third day
		SULFANILAMIDE + AUTOGENOUS SERUM					
Finland, Brown and Rauh	17	Fracture of skull; 3 negative blood cultures	XXVIII	Frequent lumbar punctures; transfusions; sulfanilamide by mouth, total 189 Gm. in 25 days; autogenous serum intraspinally	189.0	10-12	Spinal fluid culture sterile thirteenth day; anemia developed
	10	Otitis media; 1 negative blood culture	III	Mastoidectomy; sulfanilamide by mouth, total 84 Gm. in 15 days; autogenous serum intraspinally	84.0	8-10	Spinal fluid culture sterile eleventh day
		SULFANILAMIDE OR PRONTOSIL + ANTIPNEUMOCOCCUS SERUM					
Query, R. Z.: J. A. M. A. **111**: 1373 (Oct. 8) 1938	33	Pneumonia; empyema; blood culture positive	VII	Sulfanilamide, total 200 Gm. in 14 days; specific antipneumococcus serum intravenously and intraspinally	200.0	20-25	
Boyd, L. J.; Baron, B., and Schlachman, M.: New York M. Coll. & Flower Hosp. Bull. **1**: 99 (June) 1938	43	Primary? 1 negative blood culture	II	Frequent lumbar punctures; 90,000 units of meningococcus antitoxin intravenously; 117 cc. of antimeningococcus serum intraspinally; antipneumococcus serum (II) intraspinally and intravenously for 5 days; 10 cc. of prontosil (2.5%) intravenously and 40 cc. intramuscularly in 4 days	1.25	.....	Note small amount of drug used
	14	Primary? 1 negative blood culture	II	Frequent lumbar punctures; antimeningococcus serum intraspinally and intravenously; antipneumococcus serum intraspinally; 5 cc. of 0.5% ethylhydrocupreine intraspinally; 20 cc. of prontosil (2.5%) subcutaneously; 20 cc. of 0.8% sulfanilamide intraspinally	0.66	.....	Note small amount of drug used
		SULFAPYRIDINE					
Reid, G. C. K., and Dyke, S. C.: Lancet **2**: 619 (Sept. 10) 1938	7	Acute pharyngitis; blood culture not noted	..	Sulfapyridine by mouth, total 22.5 Gm. in 6 days	22.5	.....	Spinal fluid culture sterile in 24 hours
Robertson, Kenneth: Lancet **2**: 728 (Sept. 24) 1938	14	Primary? blood culture not noted	..	Felton's serum (I and II) intravenously; soluseptasine (a sulfanilamide compound), 20 cc. intraspinally and intramuscularly; sulfapyridine, total 27 Gm. in 3 days and 6 Gm. in 2 days	Soluseptasine, 20 cc.; sulfapyridine, 33 Gm.	.....	Spinal fluid culture sterile in 48 hours; hematuria developed
Cunningham, A. A.: Lancet **2**: 1114 (Nov. 12) 1938	47	Sinusitis; blood culture not noted	I	Sulfanilamide by mouth, total 15 Gm. in 36 hours; sulfapyridine, total 50 Gm. in 7½ days	Sulfanilamide, 15; sulfapyridine, 50	15	

bearing rod. Cultures of the spinal fluid were positive for Streptococcus viridans until the tenth day, at which time pneumococcus type III was observed. Spinal fluid cultures remained positive for pneumococci throughout despite a fall in the cell count. Roentgenograms of the mastoid regions showed haziness of the cells on the right; at operation pus was found in both mastoid regions. The patient became increasingly drowsy and was comatose for forty-eight hours before death on the seventeenth hospital day. Necropsy showed purulent meningitis with no evidence of sinus thrombosis or brain abscess. The patient received a total of 64 Gm. of sulfanilamide with an equal amount of sodium bicarbonate by mouth, a small amount of 0.8 per cent sulfanilamide intraspinally on eight occasions and prontosil intravenously (20 cc. on three occasions).

CASE 5.—*Pneumococcic meningitis (type III) following otitis media and mastoiditis.* M. Y., aged 7 years, had had bilateral otitis media for two weeks, frontal headache for five days and stiffness of the neck for three days. On admission there was slight stiffness of the neck, Brudzinski's sign and photophobia were present, the reactions of the pupils to light were sluggish, there were bilateral nystagmus and bilateral papilledema, the deep reflexes were hypo-active and there was dulness of the ear drums. Cultures of material from the right ear after myringotomy were positive for pneumococcus type III and from the left ear were negative. Roentgenograms of the mastoid regions were negative on two occasions. Trepanation was performed on the third day as a safeguard for lumbar punctures. A blood culture on the second day was positive for pneumococcus type III. Spinal fluid cultures were negative until the fifth day, when pneumococcus type III was found. Bilateral mastoidectomy was performed on the sixth day; on the right there were necrotic cells and pus, and on the left the cells were apparently normal. Cultures of material from the mastoid regions were negative. There was no clinical improvement. No localizing signs of brain abscess were present. The pres-

TABLE 2.—*Deaths from Pneumococcic Meningitis in Patients Treated with Sulfanilamide Compounds*

Reference	Age, Years	Probable Source of Infection	Type of Pneumococcus in Spinal Fluid	Treatment	Drug Approximate Total, Gm.	Free Sulfanilamide in Blood, Mg. per 100 Cc.	Comment
Millett, J.: J. A. M. A. **100**: 2138 (Dec. 25) 1937	53	Sinusitis; blood culture positive	III	Turbinectomy and sinus drainage; frequent lumbar punctures; prontosil intraspinally and intramuscularly, total 120 cc. (2.5%)	3	.....	Necropsy: purulent meningitis, pituitary tumor, no damage to central nervous system from prontosil intraspinally (no drug by mouth)
Finland, M.; Brown, J. W., and Rauh, A. E.: New England J. Med. **218**: 1033 (June 23) 1938	19	Primary? blood culture positive	XI	Frequent lumbar punctures; transfusions; sulfanilamide, total 105 Gm. by mouth, 3 Gm. subcutaneously, 2.5 Gm. intraspinally; fresh human serum intraspinally	110	.....	Progressive anemia developed; necropsy: purulent meningitis, frontal cortical abscess, bronchopneumonia
	47	After sinus operation; blood culture positive	XXI	Frequent lumbar punctures; transfusions; sulfanilamide by mouth, total 92 Gm. in 23 days	92	.....	No necropsy
	43	4 weeks after pneumonia; blood culture positive	VII	Frequent lumbar punctures; sulfanilamide by mouth, total 42 Gm. in 6 days; specific antipneumococcus serum intravenously; normal serum intraspinally	42	4-5	Necropsy: purulent meningitis, lobar pneumonia, vegetative endocarditis
	3	Otitis media; blood culture positive	IV	Frequent lumbar punctures; sulfanilamide by mouth, total 12 Gm. in 2 days; antipneumococcus serum intravenously (rabbit); antiserum and human serum intraspinally; mastoidectomy not done	12	.....	Moribund; died in 36 hours; necropsy: purulent meningitis, congestion of lungs
Hewell and Mitchell case 5 (chart 5)	7	Otitis media; mastoiditis; blood culture positive	III	Mastoidectomy; frequent lumbar punctures; ventricular puncture; trepanation; sulfanilamide by mouth, total 36 Gm. in 10 days and in 0.8% solution intraspinally and intravenously	36+	.....	Jaundice developed; necropsy: purulent meningitis, occipital and cerebellar abscesses, sinus thrombosis
Case 6	2 mo.	Probably otitis media and mastoiditis; blood culture positive	VII	Sulfanilamide by mouth, total 6 Gm.; ethylhydrocupreine in large doses; specific serum intramuscularly	6	.....	No necropsy
Case 4 (chart 4)	9	Otitis media; mastoiditis; blood culture negative	III	Mastoidectomy; frequent lumbar punctures; transfusions; sulfanilamide by mouth, total 64 Gm. in 13 days and in 0.8% solution intravenously; prontosil (60 cc.); at first antistreptococcus serum because Streptococcus viridans then in spinal fluid	64+	7-9	Necropsy: purulent meningitis, no abscess or sinus thrombosis

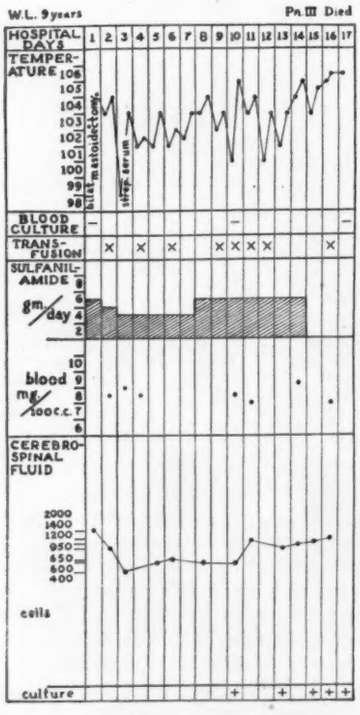

Chart 4.—Observations in case 4.

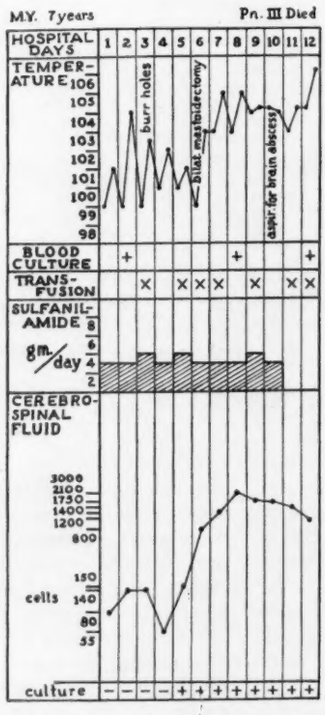

Chart 5.—Observations in case 5.

sure of the spinal fluid increased. Ventricular punctures and aspiration for brain abscess were performed on the tenth day; 10 cc. of pus was obtained through burr holes made in the right cerebellar region, and no abscess cavity was found. Icterus developed on the sixth day, and the patient died on the twelfth hospital day. Necropsy showed extensive destruction of the mastoid bone, epidural pus over the cerebellar hemisphere, extensive cerebral leptomeningitis, abscess of the left occipital lobe (small and early), thrombosis of all the meningeal sinuses and early lobular pneumonia. The patient received 36 Gm. of sulfanilamide with an equal amount of sodium bicarbonate by mouth and small amounts of 0.8 per cent sulfanilamide intraspinally and intravenously on six occasions.

CASE 6.—*Pneumococcic meningitis (type VII).* H. C., a white girl aged 2 months, was seen only casually by us and only a brief history is possible. She had had fever and been irritable for one week and had a convulsion on the day of admission. The fontanel was bulging, the ear drums were slightly dull, there was stiffness of the neck and Brudzinski's sign was present. The patient was in coma on admission. The spinal fluid showed 22,400 cells, a positive Pandy reaction and pneumococcus type VII. The blood culture was positive for pneumococcus type VII. The patient received a total of only 6 Gm. of sulfanilamide. She also received ethylhydrocupreine hydrochloride in rather large doses and specific serum intramuscularly. She died on the sixth day after admission.

SUMMARY

There are at least thirty reported cases [2] of recovery from pneumococcic meningitis, including three observed by us, in which part of the treatment consisted in the use of sulfanilamide or related compounds. It appears reasonable to conclude that sulfanilamide compounds were responsible for these recoveries in most instances, since the mortality

2. This is not a complete list, since a few reports were not available to us.

rate was so high with other forms of treatment. In a few instances the dose was so small that the effect of the drug must be considered doubtful. It is to be noted that recovery occurred with the use of different compounds, such as prontosil, sulfanilamide and sulfapyridine; that is to say, the data now available do not permit conclusions concerning the relative merit of these different compounds in the treatment of pneumococcic meningitis.

There are at least eight cases of pneumococcic meningitis, including three observed by us, in which sulfanilamide was given and in which recovery did not follow.

It could not be shown statistically that the age of the patient, the dose of sulfanilamide employed or the type of pneumococcus had any relation to recovery.

Of the patients receiving sulfanilamide who recovered, only one showed pneumococci in the blood culture; sixteen other patients had negative blood cultures, and for thirteen cultures were not reported. Of the eight patients receiving sulfanilamide who died, the blood cultures were positive for seven. This indicates that even with the use of sulfanilamide a blood stream infection with pneumococci is a factor in mortality and perhaps also that with such infection large doses of sulfanilamide should be tried.[3]

TREATMENT OF TESTICULAR DEFICIENCY WITH TESTOSTERONE PROPIONATE

E. PERRY McCULLAGH, M.D.

CLEVELAND

Testicular function is known to be intimately connected with the growth of the penis and its erectile power, the growth and maintenance of the secondary sex glands, the maturation of the skeleton and the growth, and in some species the maintenance, of the secondary sexual characteristics. Chemical substances which have pharmacologic properties similar to those of testicular extracts have been isolated from human urine and animal adrenals, and they have been demonstrated in other tissues. Such substances are called androgens. Many androgens, some of which are known to occur in nature, have been produced artificially from sterols. Koch [1] has recently published a comprehensive review of the literature dealing with these facts.

Moore's [2] experiments showed that testis extracts produced evidence of damage to spermatogenesis, and he stated that testis hormones could not be used clinically without probable harm to the production of sperm. Walsh, Cuyler and McCullagh [3] in 1933 demonstrated that androgenic urinary extracts maintained spermatogenesis in hypophysectomized rats. More recently this has been confirmed in the laboratories of the Cleveland Clinic and also by Nelson and Gallagher.[4] Although they appear to be opposed, both of these observations seem to be factual. Their clinical significance has not yet been made clear.

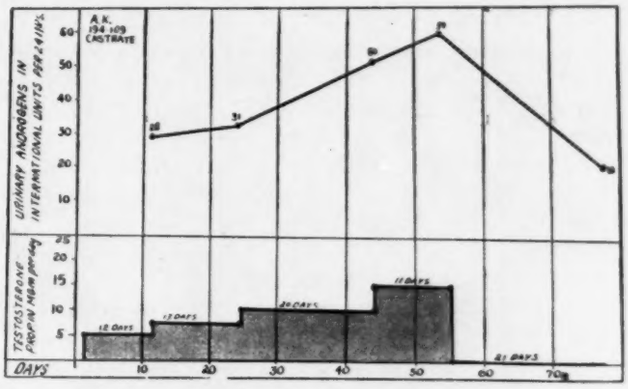

Fig. 3.—Excretion curve of a castrate aged 48.

The only androgen which has been isolated from testes is testosterone,[5] although it has not been proved that this is the only hormone of the testes or that it will completely replace the endocrine activity of that gland.

This study is concerned with the urinary excretion of androgens in the normal male, in cases of testicular deficiency and after injections of androgens. The data indicate in some degree to what extent testosterone propionate will develop and maintain the sexual organs and characteristics in the human male.

In the cases studied, particular attention has been paid to penile growth and function, the production of secondary sex characteristics, prostatic growth, production of semen, spermatogenesis, epiphysial closure and the rate of urinary excretion of injected androgens. Since only persons with definite evidence of hypogonadism have been treated, many of the patients have been impotent and it has been impossible to study the production of semen until after therapy has been instituted. For similar reasons the data regarding production of sperm are scanty.

BIO-ASSAYS FOR URINARY ANDROGENS

The most useful method of studying the hormonal activity of the testis is bio-assay based on capon comb growth. A highly accurate method and the one used in these studies is a modification of the one devised by Gallagher and Koch.[6] Brown or white leghorn capons may be used. After the urine to be extracted has been hydrolyzed by boiling with hydrochloric acid, it is extracted in a special apparatus by having benzene passed through it at a rate of from 6 to 8 liters an hour for two hours. Subsequently the benzene is distilled off, the acid neutralized and the extract dissolved in oil. The oil is injected into the breasts of five capons, and their comb growth forms the basis for computation. At the same time, for the purpose of comparison, a group of controls are given injections of standard amounts of crystalline androsterone. It has been shown

3. Since this paper was submitted we have observed another patient with pneumococcic meningitis to whom both sulfanilamide and sulfapyridine were administered. Recovery followed within a period of about three weeks. Thus we have now treated seven patients with sulfanilamide or related compounds, of whom four have recovered.

From the Cleveland Clinic.

Mr. W. Kenneth Cuyler conducted all the assays reported in this paper.

Read before the Section on Urology at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 15, 1938.

Owing to lack of space, this article has been abbreviated for publication in THE JOURNAL. The complete article appears in the author's reprints.

1. Koch, F. C.: Male Sex Hormones, Physiol. Rev. **17:** 153-238 (April) 1937.

2. Moore, C. R.: Testis Hormone, J. A. M. A. **104:** 1405-1411 (April 20) 1935.

3. Walsh, E. L.; Cuyler, W. K., and McCullagh, D. R.: Effect of Testicular Hormone on Hypophysectomized Rats, Proc. Soc. Exper. Biol. & Med. **30:** 848-850 (April) 1933.

4. Nelson, W. O., and Gallagher, T. F.: Some Effects of Androgenic Substances in the Rat, Science **84:** 230-232 (Sept. 4) 1936.

5. Laqueur, E.; David, K.; Dingemanse, E., and Freud, J.: Ueber männliches Hormon; Unterschied von Androsteron aus Harn und Testosteron aus Testes, Acta brev. Neerland. **5:** 84, 1935.

6. Gallagher, T. F., and Koch, F. C.: Quantitative Assay for Testicular Hormone by Comb-Growth Reaction, J. Pharmacol. & Exper. Therap. **55:** 97-117 (Sept.) 1935. Gallagher, T. F.; Koch, F. C., and Dorfman, F. I.: Procedures for Quantitative Extraction of Sex Hormones from Urine, Proc. Soc. Exper. Biol. & Med. **55:** 440-444 (Dec.) 1935.

recently by D. Roy McCullagh and McLin [7] that dibutyl ether is an excellent extracting solvent for androgenic substances and may be utilized with less complex equipment than benzene. Essentially the same results are obtained with the two methods.

NORMAL EXCRETION OF ANDROGENS

Normal levels of excretion of androgens are shown in table 1. The wide range of normal values both for different persons and for the same person is apparent.

The urinary excretion of androgens in normal men has been reported by Koch.[8] In twenty assays on men between 24 and 34 years of age the average number of bird units was 30, the lowest 16 and the highest 72.

The figures in table 2 demonstrate the range of androgen excretion of persons with distinct clinical evidence of hypogonadism as compared with that for normal persons. Such an assay as the one which yielded 16 units of androgens in the twenty-four hour urine of a castrate is interesting. It demonstrates clearly that not all androgens arise in the testes.

THE EXCRETION OF INJECTED ANDROGENS

The injection of testosterone propionate is followed by an increased excretion of androgens in the urine. By the use of available methods, however, it is not possible to determine what chemical substance is excreted. Such studies indicate in a general way the frequency with which injections must be given and the doses necessary to maintain normal androgen excretion. If doses of 10 mg. of testosterone propionate are injected, urinary androgens may fall to their original low levels within about three days. For example, a castrate 64 years old had had four preliminary assays, none of which showed any measurable androgen. He was given 10 mg. of testosterone propionate as oreton,[9] and twenty-four hour specimens of urine were collected, beginning from the moment of injection. The first day 16 international units was excreted, the second day 2 and the third day none. A 33 year old patient with severe hypogonadism without treatment excreted 2 units in twenty-four hours. On three days following the injection of 10 mg. of testosterone propionate he excreted 11, 7 and 2 units respectively.

If large doses are injected, the complete excretion apparently takes a longer time. A man 27 years of age had severe hypogonadism and had excreted 6.6 and 7 units of androgen per twenty-four hours before therapy. Assays indicated the excretion of 100 mg. of testosterone propionate within six days.[9a]

It is instructive to note the amounts of testosterone which must be injected in cases of hypogonadism to bring the urinary excretion to within normal range. Such doses as produce normal excretion have in the patients treated been adequate to overcome most of the evidences of testicular deficiency; symptoms have disappeared in a few days, anatomic changes requiring weeks or, in the case of severe prepuberal hypogonadism, many months. It has not been shown definitely that it is necessary to keep the urinary excretion normal in order to obtain desirable clinical effects. A male castrate 48 years of age without treatment repeatedly excreted quantities of androgens at about the lower range of normal. Figure 3 shows the consistent elevation in levels of urinary androgens with increasing doses of testosterone propionate.

RESULTS OF THERAPY FOR SEVERE PREPUBERAL TESTICULAR DEFICIENCY

Koch [8] has cited the results of Kenyon in the treatment of hypogonadism with synthetic androgens, and Hamilton [10] has reported the production of penile erections by the use of such androgens.

The most severe clinical test of the value of testicular hormone is the test of its ability to produce the evi-

TABLE 1.—*Urinary Androgens per Twenty-Four Hours in Normal Men*

Subject	Age	International Units: Benzene Extraction	International Units: Dibutyl Ether Extraction
1	27	25	35
2	29	86	
3	37	42	76
		43	
4	28	51	24
			35
			18
5	30	21	
6	33	32	22
		16	22
7	33	46	54
8	23	34	23
			42
			77
9	32	41	
10	23	61	33
			55
			45
11	28	..	18
12	29	29	
13	25	33	
14	29	50	33
15	28	37	
16	29	..	28
			38
17	32	..	24
18	27	..	25
19	27	..	44
20	26	..	18
			19
Average		40.5	35.1

TABLE 2.—*Excretion of Androgens in Hypogonadism*

	Age	International Units Excreted in 24 Hours
Prepuberal hypogonadism without other signs of pituitary disease	20	9
	21	16, 13
	52	0, 1, 2
	30	23
	26	7, 14
	33	2, 8, 11, 7, 2
	34	2, 0
	31	0, 0, 0, 2, 1, 0
	23	2, 6, 5
Fröhlich's syndrome	23	10
	23	34
	13	3
	14	4
	14	0
	19	0, 0
	13	8
Dwarfism and hypogonadism	19	0, 9
	20	10
Gigantism and hypogonadism	20	5
Adult castrates	64	0, 0, 0, 0
	52	7
	42	16, 0, 10

7. McCullagh, D. R., and McLin, T. R.: Extraction of Androgens from Urine, Endocrinology **22**: 120-121 (Jan.) 1938.

8. Koch, F. C.: Biochemistry and Physiological Significance of Male Sex Hormones, J. Urol. **35**: 382-398 (March) 1936.

9. Oreton is the trade name of a solution of testosterone propionate in oil produced by the Schering Corporation and supplied for these studies through the courtesy of Dr. Irwin Schwenk and Dr. Max Gilbert.

9a. This work is being reported in greater detail in Endocrinology (to be published).

10. Hamilton, J. B.: Induction of Penile Erection by Male Hormone Substances, Endocrinology **21**: 744-749 (Nov.) 1937.

dences of normal function of testis hormone in persons who have had severe hypogonadism from before puberty to well into adult years. Six cases of such hypogonadism have been selected for this report, together with one case illustrative of what I believe to be functional hypogonadism and one case illustrating the effect of testicular hormone in an adult castrate. All of the patients with prepuberal hypogonadism received gonadotropic hormone therapy for several months with pregnancy urine extracts, pituitary extracts or a combination of these. In these cases the effect of the gonadotropic substances ranged from no observed change to mild symptomatic and very slight anatomic changes. In other instances such therapy has produced good results, and it is possible that larger doses might have been followed by better results in some of these cases, depending on the amount of reactive testis tissue present. In all instances, when testosterone propionate therapy was begun it was the only androgenic substance used. Thyroid therapy was used in two cases (3 and 5). Two of the cases are reported in some detail and illustrate well the type of change seen in the others, the more important data of which are reported:

CASE 1 (fig. 4).—A man aged 23 complained in 1934 of lack of normal development. At the age of 15, because of cryptorchidism and pain, bilateral orchidopexy had been attempted, after which both testes atrophied. He had been less active

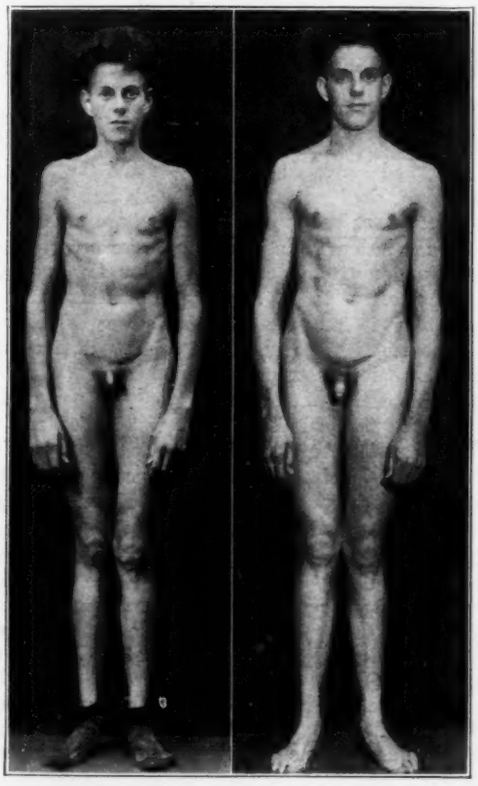

Fig. 4.—Patient 1 at 23 years and at 27 years. The development, including an increase in maturity of the facial expression, an increase in the breadth of the shoulders and development of the genitalia, is apparent. This patient had received 3,220 mg. of testosterone propionate in the fifteen months before the second photograph was taken.

than the average youth. The sexual libido was minimal; masturbation, however, was practiced about monthly, apparently with orgasm but no ejaculate. The teeth had been well formed, but some cavities developed. He had grown 3 inches (7.6 cm.) in height between the ages of 20 and 23 years.

Examination showed a person with the facial expression of a boy of 14 years. His voice was puerile. He was slender, with long hands and feet. His height was 65¾ inches (167 cm.) and his weight was 107 pounds (48 Kg.). His span (both arms extended) was 70½ inches (179 cm.) and the symphysial height was 36¼ inches (92 cm.). The skin was normal in texture, and the trunk and limbs were almost hairless except for about fifteen pubic hairs. The penis was preadolescent in type, measuring less than 4 cm. from as close as the finger could be

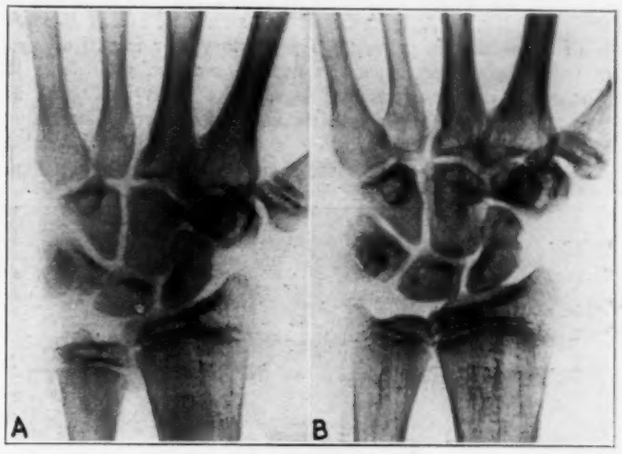

Fig. 5 (case 1).—*A* shows an epiphysial age of 16 years, the chronologic age being 23 years. *B*, chronologic age 27 years; after marked puberal changes following treatment, the epiphysial maturity is unchanged.

pressed to the pubis to the end of the prepuce. The prostate was minute and flat, and it was questionable whether its borders could be defined by palpation. The small, pale scrotum contained two very soft pea-sized testes.

During 1934 and 1935, seven assays showed measurable traces of urinary androgens. No gonadotropic substance was demonstrated in the urine by the modified Friedman test. Six metabolism tests in 1934 and 1935 averaged —9 per cent. Blood counts, apart from showing a slightly low red cell count gave

TABLE 3.—*Therapy in Case 1*

1935	July to January 1936	Prephysin	1 cc., 6 doses a week
1936	January to March	Prephysin plus antuitrin-S	1 cc. } 6 doses 0.25 cc. } a week
	March 18 to May 6	Androsterone	2.5 mg. every 2d day
	May 8 to November 30	Testosterone (plain)	2.5 mg. daily
	December 16 to Feb. 10, 1937	Testosterone propionate	5 mg. 3 times weekly
1937	Feb. 10 to April	Testosterone propionate	10 mg. 3 times weekly
	August to May 17, 1938	Testosterone propionate	20 mg. 3 times weekly

normal results. Urinalyses and examination of the blood sugar and blood cholesterol gave normal results. A trace of creatine was excreted on one of four occasions. The creatinine excretion was normal.

The sella turcica was normal to roentgen examination. The skeletal age estimated from the development of the epiphyses was just over 16 years.

The therapy is shown in table 3. The total dose of testosterone has been 3,715 mg.

While gonadotropic substance was being administered, repeated assays failed to show any rise in the level of excreted androgens and no symptomatic or anatomic change was noted. After the patient had received testosterone until August 1936 there were some penile growth (6 cm.) and a questionable increase in the axillary and pubic hair, and erections were more frequent. This therapy also failed to raise the level of excreted androgens.

Immediately after the institution of testosterone propionate therapy, a twenty-four hour excretion of 28 units of androgen was found. Erections occurred daily or oftener. By February 10 a small ejaculate had occurred. With 10 mg. every second day, 26 and 27 units of androgen were excreted. By

April the penis was 8 cm. in length, the prostate was enlarging and the scrotum was more pendulous. In July nocturnal emissions began to appear about every three weeks.

The voice became decidedly deeper, and the appearance and demeanor were more mature. The patient has continued to grow in height, and the shoulders are broader. His present height is 69 inches (175 cm.), his span 75 inches (190 cm.), his symphysial height 38 inches (96 cm.) and his weight 133 pounds (60 Kg.). A light beard has appeared, and a puberal type of facial acne is present. The axillary hair is still sparse. The pubic hair approaches the normal amount, and there is obvious hair on the arms and legs. The penis is 10 cm. in length and the scrotum larger, thicker and darker. The testes have not enlarged. The prostate is about 3 cm. in width and from 2 to 3 cm. in height. Erections and nocturnal emissions

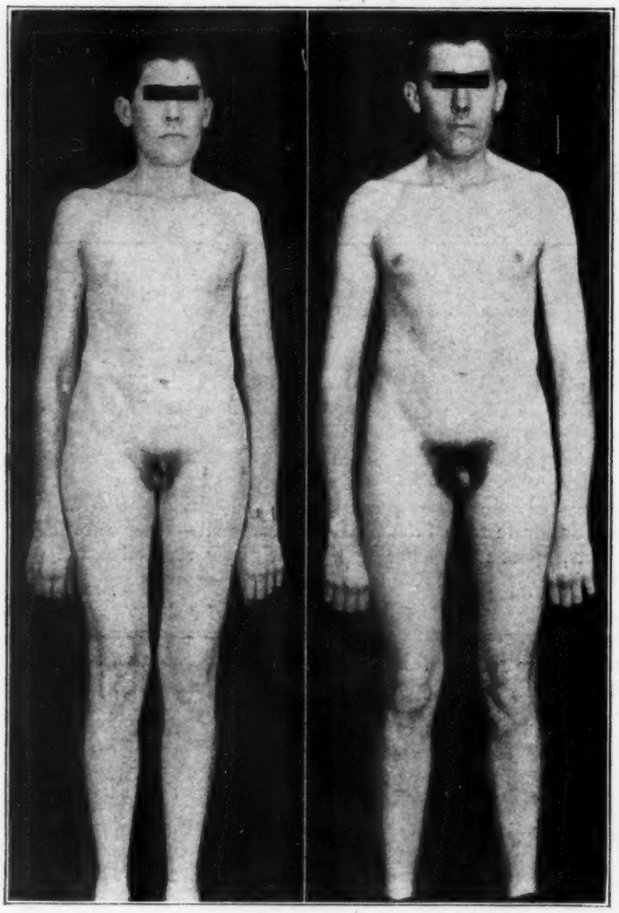

Fig. 6.—Patient 2 Dec. 24, 1936, and April 16, 1938. He had received 3,560 mg. of testosterone propionate in the intervening sixteen months.

occur normally. The ejaculate contains no sperm, is highly mucoid and has a volume of 1.5 cc. The blood count is unchanged; the blood sugar, calcium and phosphorus levels remain normal and unchanged, and the blood cholesterol content is 120 mg. per hundred cubic centimeters. The basal metabolic rate is —9 and —13 per cent. An extremely interesting feature is that the epiphysial development has remained unchanged; the epiphysial lines, for instance at the lower end of the radius and ulna and at the proximal end of the first metacarpal, are as widely open as in 1934 (fig. 5). This demonstrates that testosterone propionate, capable of producing most of the evidences of puberty, is alone not the substance which causes epiphysial closure, ordinarily considered an integral part of puberal maturity, or that larger doses are required to affect this function. It should be noted that the patient received no thyroid therapy.

CASE 2 (fig. 6).—A white man aged 30 who complained Dec. 19, 1936, of failure of genital development had had mumps at the age of 8 years. His appearance was typical of eunuchism; his height was 68½ inches (174 cm.), and his span was 75½ inches (192 cm.). The voice was high, there was a slight down on the cheeks and the axillary and pubic hair was very scant. The penis and prostate were infantile, and pea-sized testes were palpable. Erections occurred at about monthly intervals. There were no clinical evidences otherwise of pituitary or thyroid disease.

He had mild microcytic anemia. The basal metabolic rate was —21 per cent, and the blood cholesterol content was 190 mg. per hundred cubic centimeters. Examination of the visual fields and roentgen examination of the sella turcica gave normal results. The epiphyses at the lower end of the radius and ulna and the crest of the ilium were incompletely closed. There was well developed hypertrophy of the radial epiphysis (the patient was a sign painter).

The Friedman test showed no evidence of gonadotropic substance. A urinary androgen content as high as 23 units per twenty-four hours was found before treatment. Between Feb. 6 and April 10, 1937, he was given 6,200 units of gonadotropic substance. February 27 the urinary androgen content was 2.1 units. There was slight increase in testicular size and some improvement in the sense of well being.

April 10 the administration of testosterone propionate 10 mg. every second day was begun. This was increased to 20 mg. every second day August 1 and to 30 mg. at the same intervals August 21 and has been 25 mg. three times weekly since November 1937. The total dose of testosterone propionate has been approximately 3,900 mg.

When this therapy was begun, erections occurred promptly and appeared three or four times daily. In August the first nocturnal emission occurred, the voice was lower, the scrotum was more pendulous and the prostate was distinctly larger. In September facial acne appeared. The urinary androgen content was 74 units in August, 64 units in October and 40 units in March 1938.

Semen specimens measured 0.8 cc. in August 1937, 2.7 cc. in February 1938 and 1.7 cc. in April 1938. There were no sperms.

By April 1938 the facial appearance was more mature, the beard had increased visibly, requiring shaving every third day, the body hair had increased considerably and the axillary and pubic hair approached normal. The voice had become much lower. The shoulder breadth appeared to have increased. The penis was 8 cm. in length and erections were occurring several times a day and nocturnal emissions every few weeks. The prostate had grown to a size approximating normal for the age of 18 or 19 years, the median sulcus still being well marked. The testes were distinctly smaller than at the end of the gonadotropic substance therapy.

In May the basal metabolic rate was —5 per cent. The epiphysial line at the end of the ulna was closed and that of the radius appeared to be closed but the line could be distinctly seen. The epiphysis of the iliac crest was still ununited. It would appear that in this case the rate of epiphysial closure was hastened somewhat during therapy.

CASE 3 (fig. 7).—A man aged 27 who in May 1936 complained of arrested sexual development was rather obese and showed all the evidences of severe prepuberal hypogonadism. There was no history suggestive of testicular injury. He had the appearance of a boy of 16. His height was 67½ inches (171 cm.) and his span 71¾ inches (182 cm.). He weighed 156 pounds (71 Kg.) The voice was high. There were a few pubic and axillary hairs but no beard. The penis was 1 inch (2.5 cm.) in length and the small scrotum held no palpable testes. The prostate was not palpable.

The sella turcica was normal to roentgen examination, and the visual fields and dextrose tolerance were normal. There was slight microcytic anemia. The blood cholesterol content varied between 128 and 150 mg. per hundred cubic centimeters. Four basal metabolic rates averaged —10 per cent. The epiphysial age was approximately 18½ years, the phalangeal epiphyses being closed. The Friedman test gave a negative reaction, and the urinary androgens measured 6 international units in twenty-four hours.

In 1934 three basal metabolic rates had averaged —5 per cent and the blood cholesterol content was 126 mg. per hundred cubic centimeters. At that time the epiphysial lines of the

phalanges were incompletely closed. The bone age had been estimated to be 16½ years by Dr. T. W. Todd and a diagnosis of hypothyroidism arrived at from roentgen evidence alone.

From October 1934 to August 1935 the patient had received 100 units of gonadotropic substance three times weekly with no benefit. Thyroid in varying doses was used from January to August 1935. The therapy since June 1936 is outlined in table 4. The total dose of testosterone propionate has been 5,260 mg. in seventeen months.

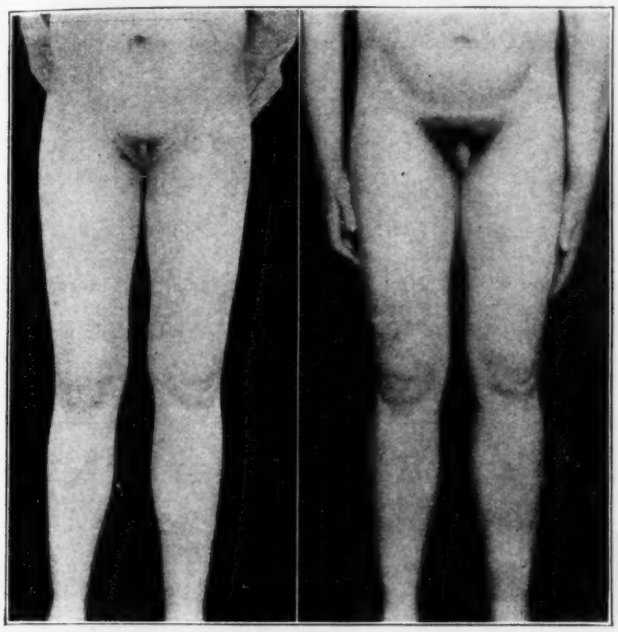

Fig. 7.—Patient 3 May 14, 1936, and May 4, 1938. He had received testosterone propionate for sixteen months before the second photograph was taken.

While the patient was taking androsterone and testosterone, the urinary androgen content varied from 3 to 4 units and erections increased slightly. A slight, glairy secretion was seen at the urethral meatus, and the only anatomic change noted was slight penile growth.

TABLE 4.—*Therapy from June 1936 in Case 3*

1936	June 12 to Aug. 1	Androsterone 2.5 mg. every second day
	Aug. 19 to Nov. 25	Testosterone 2.5 mg. every second day
	Nov. 26 to Dec. 16	Testosterone 5 mg. every second day
	Dec. 17 to Jan. 9, 1937	Testosterone propionate 5 mg., 6 doses a week
1937	January 11	Testosterone propionate 15 mg., 6 doses a week
	February 11	Testosterone propionate 10 mg., 3 doses a week
	May 3 to May 24	No therapy
	May 24 to July 27	Testosterone propionate 10 mg., 3 doses a week
	July 27 to Aug. 18	No therapy
	Aug. 18 to Oct. 18	Testosterone propionate 20 mg., 3 doses a week
1938	Oct. 18 to May 1938	Testosterone propionate 50 mg., 3 doses a week

With the patient receiving testosterone propionate, an androgen assay in December 1936 showed 21 units. By January 19 assays showed a content as high as 119 units. Erections occurred three or four times daily. A small ejaculate was present. The penis had increased to 3 inches (7.6 cm.) in length, and axillary and pubic hair had increased. When treatment was discontinued, the number of erections and the amount of ejaculate diminished markedly within ten days.

By April the ejaculate had increased further, axillary and pubic hair were increasing visibly, the scrotum was larger and darker and the penis measured 3½ inches (9 cm.) from pubis to tip of prepuce. In August the voice was decidedly lower.

In October 1937 the ejaculate measured 0.4 cc.; in November 1937, 0.8 cc., and in January 1938, 0.5 cc. Nocturnal emissions occurred every two or three weeks. The results of blood counts, the serum calcium, phosphorus and cholesterol contents and the metabolic rates have not changed. In May 1938 the epiphysial age had advanced to 21 years. The epiphysial development has therefore advanced at about a normal rate during the past four years but has apparently not exceeded the normal rate in spite of the large doses of testis hormone given. The testes have not become palpable.

At the present time axillary and pubic hair approach normal. The beard has increased slightly, and hair is appearing on the arms and legs. The voice is decidedly lower. The penis is 3¾ inches (9.5 cm.) long. The prostate has increased little if at all in size.

CASE 4. (fig. 8).—A man aged 31 who in May complained of underdeveloped genitalia had no history suggesting testicular damage. The libido was minimal, there were no nocturnal emissions and erections were rare.

TABLE 5.—*Therapy in Case 4*

	Date	Medication	Assay
1936	May 12 to June 16	Testosterone 2.5 mg., 3 times a week	0.0
	June 16	Dihydroandrosterone 2.5 mg., 3 times a week	
	July 20	Testosterone 2.5 mg., 3 times a week	0.0
	October 6	Testosterone 5 mg., 3 times a week	2.4
	November 1		1.0
	November 15		0.0
	December 1	Testosterone propionate 5 mg., daily	
	December 16		32.0
1937	January		
	April		
	September 21	Testosterone propionate 10 mg., daily	10.0
	December 6		15.5

At the age of 20 years his height was 65½ inches (166 cm.), and at the time of my examination, ten years later, it was 67¼ inches (171 cm.). The weight was 162 pounds (73 Kg.), the span 71½ inches (182 cm.) and the symphysial height 36 inches

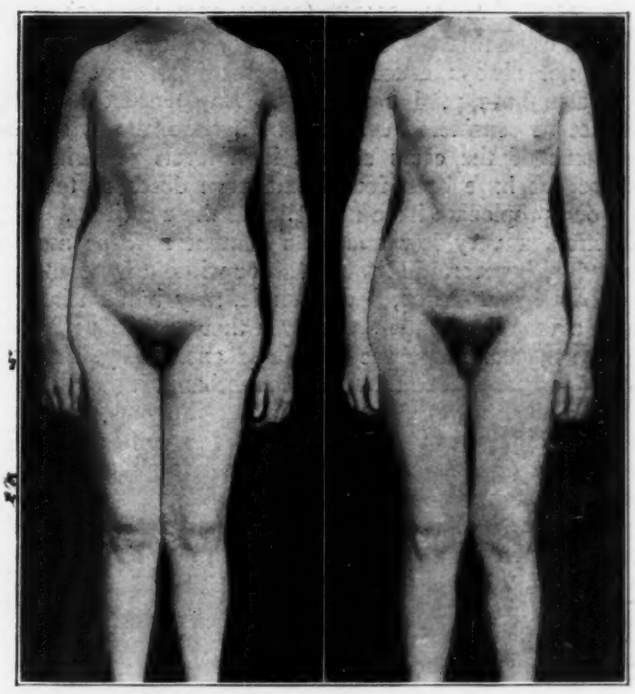

Fig. 8.—Patient 4 Dec. 7, 1936, and March 28, 1938. He had received 2,845 mg. of testosterone propionate in the fifteen months before the second photograph was taken.

(91 cm.). The voice was high and the face and body were hairless, but there was sparse axillary and pubic hair. The penis was very small, appearing 1 inch in length though actually it was 2¼ inches (5.7 cm.) when measured by pressing the rule against the pubis. The prostate was minute. The scrotum was very small, and the testes were the size of small peas.

The basal metabolic rate was —27 per cent, but there were no clinical evidences of hypothyroidism. The blood cholesterol content was 176 mg. per hundred cubic centimeters and later varied between 120 and 145 mg. on several occasions. The epiphysial age was 20 years. Assays for urinary androgens showed none. Roentgen examination of the sella turcica had given normal results repeatedly, and the visual fields showed no evidence of suprasellar lesions.

Treatment previously had included from 1 to 2 cc. of gonadotropic substance in the form of antuitrin-S three times weekly for five months, with slight improvement. The treatment with testis hormones is outlined in table 5. The total dose of testosterone propionate was 2,845 mg. in seventeen months.

Within a few days of the beginning of therapy erections increased, and by July they were occurring several times daily. In October 1936 the penis had increased 2⅞ inches (7.3 cm.) in length and there was a slight viscid secretion at the meatus. In January 1937 facial acne of the puberal type was present, the voice had become decidedly lower and there was distinct though slight increase in the beard. The prostate was palpably larger but still smaller than normal. The penis measured 3⅞ inches (9.9 cm.) in length and coitus was normal. The rate of progress was obviously faster with testosterone propionate than with other types of treatment used.

Cessation of injections for two and one-half weeks led to disappearance of the facial acne, lessening of the libido and potency and a slight decrease in the number of erections. By March 1938 the voice was distinctly low, the beard had increased visibly and the axillary and pubic hair were about normal. The scrotum was still small. The penis had increased to 4¼ inches (10.8 cm.) from pubis to tip. Frequent erections persisted. The prostate measured about 1½ by ¾ inches (3.8 by 1.9 cm.) as judged by palpation. The testes were unchanged in size. The epiphysial age had just reached 21 years. The ejaculate was sperm free and had a volume of 4 cc.

THE QUESTION OF FUNCTIONAL HYPOGONADISM IN THE ADULT MALE (MALE CLIMACTERIC)

It is clear that testicular deficiency of severe degree does not always cause many symptoms, since some castrates have mild complaints. Impotence in itself cannot be considered evidence of hypogonadism, since in some of the cases studied high levels of urinary androgens have been found and large doses of testosterone propionate have not relieved the condition. In addition, a very low androgen content may be associated with general ill health with or without impotence. Arterial hypertension, for example, may be associated with a very low content, and even though this is raised to the normal range the associated excitability, irritability and impotence may remain unchanged. In some adult males, however, there may be symptoms suggestive of hypogonadism, a low androgen content being associated or unassociated with testis atrophy, and the use of testosterone propionate alone may be followed by complete symptomatic relief. The following is an example of such a case:

CASE 7.—A man aged 58, first seen in February 1934 complaining of irritability, excitability and melancholia, was almost completely impotent. There was slight diffuse thyroid enlargement. The blood pressure was 110 systolic and 70 diastolic. The prostate was mildly enlarged. The testes were rather small, quite soft and associated with bilateral hydrocele. Blood counts, Wassermann tests and the sugar and cholesterol values were normal on repeated examinations. Four basal metabolic rates ranged from +5 to —12 per cent. A positive Friedman reaction was found on three of eight occasions. In August 1936 there were no urinary androgens, and in October the content was 3 units. Throughout 1934 and 1935, treatment, including the use of desiccated testis tissue and injections of hombreol, a urinary androgenic extract, did not improve his symptoms. From December 1935 to December 1936 mild improvement was noted while he was using dihydroandrosterone or testosterone 2.5 mg. every second day. The nervous symptoms were less and erections occurred occasionally. In December 1936 he began to take testosterone propionate 2.5 mg. every second day. In approximately two weeks he found himself sexually normal with great diminution in the sense of melancholy and irritability. With 2.5 mg. doses of testosterone propionate, assay showed 10 units of urinary androgens, with 5 mg. doses 18 units, with 10 mg. doses 22 units and with 20 mg. doses 80 units in twenty-four hours. Treatment was continued for sixteen months and during this period there was only the slightest possible suggestion of depression at times. Sexual potency has remained normal. At the date of writing, placebo substitution has been used for seven weeks without recurrence of symptoms.

CASTRATION

The symptoms of castration in the male may be completely relieved by injections of testosterone propionate if given in sufficient doses:

CASE 8.—A man aged 64 presented himself in November 1936 complaining of extreme "nervousness, hot spells and loss of sexual power." In May 1934 he had complained to a surgeon of bilateral testicular pain. Bilateral orchidectomy was advised and the patient was led to believe implicitly that his potency would be unchanged and that no other symptoms would occur. Within a week hot flashes identical with those seen in the female

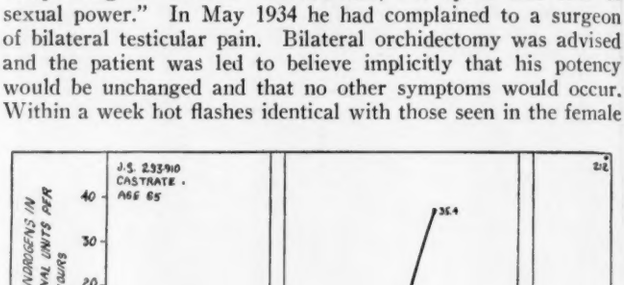

Fig. 9.—Data in case 8.

climacteric began to appear together with a sense of oppression in the chest and head, melancholia and a sense of trembling. Within a month the ejaculate was less and in two months the libido was diminished and the potency lost. Since that time there had been a constant sense of excitement, tension and giddiness. Hot flashes increased to between twelve and thirty a day, and insomnia occurred. Prostatectomy was performed in September 1934, although apparently no symptoms of obstruction were present.

Physical examination revealed a well preserved man of 64. He appeared apprehensive and excited. As he sat in the examining room, he would suddenly become restless and marked redness of the face would appear, last for about a minute and be followed by profuse perspiration. The systolic blood pressure varied from 144 to 173 and the diastolic from 80 to 100.

There was evidence of mild arteriosclerosis. The fact that the prostate felt small was probably insignificant. The vibratory sense was diminished bilaterally below the knees; other sensations and the reflexes were normal. Blood counts, urea, calcium, phosphorus and blood protein values and Wassermann tests were normal. Urinalysis showed a little albumin and a few hyaline casts. The urea clearance was normal. The blood cholesterol content was 288 and 285 mg. per hundred cubic centimeters. Dextrose tolerance following the ingestion of 100 mg. of dextrose was as follows: fasting 102, one-half hour 230, one hour 265, two hours 207, three hours 98 and four hours 68 mg. The sella turcica was normal to roentgen examination; the basal metabolic rate was ±0 per cent. Friedman tests were done on five occasions; one reaction was

positive. Figure 9 indicates the levels of urinary androgens, the doses of testosterone propionate and, in a general way, the symptomatic improvement.

November 23 the daily administration of 5 mg. of testosterone propionate was begun. For five days there was no change, after which a reduction in hot flashes was noted. No rise in urinary androgens was measured until December 18, in spite of increased doses. An erection occurred after one week of therapy. An acute infection of the respiratory tract caused a temporary increase in symptoms. By December 9 hot flashes were occurring only about four times daily. In Februrary the mental unrest and melancholia were much diminished. Normal coitus was possible once or twice a week. There was a normal orgasm but no ejaculate. At the end of February, treatment was omitted for a week; toward the end of this time all symptoms were returning, and they continued to increase for several days after the resumption of 10 mg. of testosterone propionate a day. By March sleep was normal and no sedation was necessary.

An increase in the dose produced an interesting effect, reported in July 23, 1937, by the patient's physician, Dr. E. C. McDonald: "Mr. S. was given 25 mg. of testosterone propionate June 17, and since that time he has received three ampules weekly. He has improved materially, both subjectively and objectively, with larger doses. Objectively, I am impressed by the fact that he is more alert mentally; in fact, I believe he is entirely without his former tendency to melancholia and complains of nothing, which is unusual for him. Subjectively, his libido is normal and he is able to perform sexual intercourse satisfactorily. The hot flashes gradually diminish from an average of four or five in twenty-four hours to a present level of not over two and usually one in the same length of time, these being milder and of shorter duration." He remained almost symptom free with 10 mg. doses three times a week until about March 1, 1938, when impotence recurred. Between April 4 and May 4, injections of oil were given and care was taken not to place leading questions. The impotence persisted, but little complaint of general symptoms was made. May 4, 25 mg. of testosterone propionate was given and between then and May 18 a total of 95 mg. May 6 polyuria was noted, and May 9 the first erection for two months occurred and the patient volunteered that the hot flashes had again become less severe and the "nerves steady." Subsequently, with doses of 10 mg. three times weekly potency has been maintained.

SUMMARY

In cases of severe prepuberal hypogonadism, injections of testosterone propionate in the doses indicated have been followed by symptomatic and anatomic changes in approximately the following order: Penile erections occur promptly, and there is an increase in the pubic and axillary hair. The penis grows rather markedly and the scrotum less so, and the prostate growth appears to lag perceptibly in proportion. There has been no consistent evidence of increased testicular size, although the testes appeared to be larger after treatment in case 5. Nocturnal emissions occur and the quantity of semen increases. No diminution in sperm count or inhibition of sperm production has been obvious where sperms are present, though this may not be so in cases in which there is a normal number of spermatozoa before therapy. The larynx grows and the voice becomes lower. Facial acne appears and the beard grows. Epiphysial closure has not exceeded its expected normal rate in cases in which testosterone propionate alone was used and in one case has not increased in four years in spite of marked advance in puberty. No constant change in basal metabolism has been observed. In cases of functional hypogonadism in the adult this treatment has been followed by complete relief of nervous and sexual symptoms. In castrates, nervous and vasomotor symptoms and impotence can be abolished by sufficient doses.

ABSTRACT OF DISCUSSION

DR. H. L. KRETSCHMER, Chicago: I was interested in the results of the assay by the two methods that Dr. McCullagh mentioned and to know just what takes place when these extracts are given. His results are very striking, and if this method can be used to stimulate the growth of the external genitalia it may have a definite field of usefulness. However, I think it might be desirable at this time to know what the effect of these drugs is on spermatogenesis. I believe that one may be justified in calling attention to the possible inherent dangers in some of these drugs. The point I wish to raise is that, while this drug has a certain field of usefulness, its indiscriminate use might possibly be attended by some undesirable consequences. Interesting in his experience is the fact that all the changes which occurred following the use of this drug were external, resulting in changes in the external genitalia, the growth of hair and the like. This subject, as Dr. McCullagh stated, is still a debatable one. Koch called attention to the fact that this drug may have a deleterious effect on the spermatogenic function, and this it seems to me is an important point to bear in mind. I believe that the indiscriminate use of this drug should be discouraged until its effect on spermatogenesis has been definitely established. If, for example, this drug does have a deleterious effect on spermatogenesis, undesirable results may follow its use. I think it should be emphasized that this drug should be used under careful supervision in well selected cases. Some of the undesirable effects of the treatment of undescended testes with various endocrine preparations are beautifully illustrated in the exhibit of Drs. Thompson and Heckel at the Scientific Assembly. I believe it would be most unfortunate if the indiscriminate use of this drug should be followed by interference with spermatogenesis.

DR. GEORGE G. REINLE, Oakland, Calif.: This is a subject that we still do not know a great deal about; also there is danger in its being used promiscuously. Dr. McCullagh's study has been gaged by the excretion of androgen. He has defined androgen as a chemical substance which can be found in human urine and which has pharmaceutic properties similar to testicular extract. At present there is too little evidence for one to state definitely what cells in the body secrete the substances. That these substances may be found in the urine of a patient without testicular tissue has been exemplified by the case of castration cited in which these substances were found in the urine in quantities equal to those found in normal persons. Since early Biblical times it has been known that testicular functions are related to what are termed secondary sex characteristics. In spite of exhaustive research toward ascertaining the exact nature of this relationship, the problem is by no means solved. Today there is much dispute among certain workers regarding the function and secretion elaborated by such testicular cells as the cells of Leydig and of Sertoli. It has been shown quite convincingly that testosterone propionate given to young male chicks markedly increases the growth of the comb and markedly accelerates the time at which the young roosters exhibit definite signs of masculinity. Hamilton, in a recent talk to the Western Branch of the American Urological Association, showed a movie which exhibited evidence to the effect that testosterone propionate stimulated penile growth, pubic hair and erectile power in young persons with subnormal sex characteristics. Reports of studies with the injection of substances such as testosterone have been followed by the clinical use of this substance by many physicians for such complaints as impotence and cryptorchidism. The results in cryptorchidism are very difficult to evaluate because many retained testicles descend of their own accord as the patient grows older. As Dr. McCullagh has pointed out, impotence cannot be considered evidence of hypogonadism. Although impotence may be due to the pathologic physiology of certain endocrine glands, it is often functional. Necessarily, any experimental work which is of value in increasing our knowledge of these subjects necessitates very diligent and thorough observation and a most careful analysis of the results found by the investigators. For these reasons I am particularly indebted to Dr. McCullagh for his study of the treatment of testicular deficiency with testosterone propionate. He is to be complimented for his splendid work.

DR. R. V. DAY, Los Angeles: Testosterone is a potent drug. If one is to get physiologic results, one usually gets them fairly promptly. The cases that Dr. McCullagh reported, of course, are examples of substitution therapy, and whether or not one obtains spermatogenesis or whether one produces erections or in some way relieves the impotence, I don't think matters very much, but there must be some metabolic phenomena. Perhaps they have something to do with the creatine anabolism. Certainly the patients experience a sense of well-being, that is in the cases of nervous exhaustion, asthenias and depressed energy states, and in those cases it is very useful if one does not expect too much from it. In artificial menopause in which there were severe symptoms there have been quite a number of patients who did not respond to estrogenic substances but did respond promptly to testosterone propionate. One of the advantages of the propionate salt is that it is slowly absorbed over a period of days so that larger doses may be given and need not be administered so often. I have sometimes given 100 mg. a week. Its use is so recent that there is not yet enough clinical background for a thorough evaluation of its usefulness, and there will not be for perhaps the next ten or twenty years. It is very useful in early prostatism to relieve the irritability when infection has not yet occurred and the residual urine is of no great consequence. In such cases it does not make much difference what is done as regards its effect on the spermatogenic cells for the reason that in the case of these old men it is simply a replacement therapy. In the case of impotence one should use caution and not administer the drug over a considerable period, because in animals it has been demonstrated that degeneration of the spermatogenic cells in the tubules follows the intensive administration of testosterone if it has been continued too long.

DR. L. F. HAWKINSON, Brainerd, Minn.: After considerable experience with the use of androgen during the past three years, I can confirm what Dr. McCullagh has said. It is becoming increasingly evident that the doses formerly used were inadequate. The original doses of 1 mg. produced no results; 5 mg. ampules produced some fairly good results. Since I have increased my doses to 25 mg. two or more times a week my patients are responding with more regularity, and I want to call particular attention to the fact that Dr. McCullagh used from 2,800 to 3,250 mg. in treating these patients. Many so-called androgenic preparations in my experience have been of no value. Two years ago I tested nine so-called androgenic preparations on white leghorn capons. Some of these products were labeled in capon units. It is noteworthy that the capon test proved seven of them to be worthless. Two preparations of testosterone propionate, made synthetically, were very potent. Concerning impotence, only about 20 per cent of my patients have obtained relief after injections of androgen. It is possible that I am using inadequate doses; this is suggested by Dr. McCullagh's report. I have treated more than 100 patients with androgenic substance for prostatic hypertrophy. Although I am not prepared to report the results at this time, I have this much to say: Excluding two or three patients, there was a definite increase in well-being in these older men. They not only feel better but they are more active physically, more alert mentally and the nervous symptoms are usually ameliorated.

DR. E. PERRY MCCULLAGH, Cleveland: I agree with Dr. Kretschmer that caution should be employed in the use of these materials in patients in whom any spermatozoa are present or in whom spermatogenesis is normal. There are already some data which suggest that injected androgens do not harm spermatogenesis in the rat; whether or not this will be borne out for man remains to be established. It was shown by Dr. Roy McCullagh in 1933 that in hypophysectomized rats the injection of urinary androgens extracted from male urine would maintain not only the prostate, vesicles and Cowper's glands but also the testes and spermatogenesis. At that time this work was not generally accepted. Later, however, it was adequately corroborated for testosterone propionate and other artificial androgens. This work was done in our own laboratory as well as by other workers, notably Nelson, who recently corroborated fully that these materials given in large enough quantities to animals having no pituitary glands to maintain their testes will not only do no damage but will actually maintain the spermatogenic elements. The exact mode of action of androgens under these circumstances is not entirely clear. Cutuly favors the idea that scrotal maintenance may be of primary importance, but Nelson feels that the degree of maintenance of spermatogenesis and of the scrotum do not parallel each other and are probably not interdependent. Whether or not androgens will prove valuable clinically in producing spermatogenesis must remain for future work to determine. The treatment of impotence is difficult. Certain patients who have been impotent with no signs of hypogonadism and quite high levels of urinary androgens have been treated in spite of the high androgen levels, but with no improvement. On the other hand, certain patients with impotence and low levels of urinary androgens, which we believe are the result of poor general health have not been consistently improved even when urinary excretion has been raised to high levels. There is a group of patients with impotence, however, as I indicated, who have testicular deficiency as judged from the low level of urinary androgens, and in this group treatment with testosterone propionate brings about more consistent and more pronounced improvement.

SULFANILAMIDE TREATMENT OF ERYSIPELAS

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Bellevue Hospital annually treats about 600 patients with erysipelas. Prior to 1937 the treatment of this disease was varied and not particularly effective. Erysipelas antitoxin, ultraviolet rays and local treatment of various kinds had all proved to be more or less ineffectual.

With the advent of sulfanilamide (prontylin and its related compound prontosil [the disodium salt of 4-sulfamidophenyl-2′-azo-7′-acetylamino-1′-hydroxynaphthalene-3,6′disulfonic acid]) new hope was held for controlling this disease. Enough has been said and written about these drugs to preclude any detailed discussion of their action here. Their effect on hemolytic streptococci and other bacteria is by now well known.

TABLE 1.—*Patients Treated with Sulfanilamide*

	Adult			
	Male	Female	Children	Average
Total cases treated	219	94	31	
Day of hospitalization	6.9	6.9	5.5	6.8
Days of fever	4.2	4.4	2.9	4.1
Deaths	4	1	4	
Mortality	1.82%	1.06%	12.9%	2.62%

Beginning Jan. 1, 1937, all patients with erysipelas entering Bellevue Hospital were treated with sulfanilamide (prontylin and its derivative prontosil; prontylin in tablet form for oral use and prontosil for intramuscular injection). At first dosage was a problem, but in a short time a definite plan of treatment was formulated and has been adhered to in almost all cases. This is as follows:

1. For children up to 2 years of age, two or three 5 grain (0.3 Gm.) prontylin tablets are given every day and continued daily until the temperature reaches normal. The tablets are usually crushed and given with food or fluids.

2. For children from 2 to 5 years of age, two 5 grain prontylin tablets are given three times a day (a total of 2 Gm.) and discontinued forty-eight hours after the temperature has reached normal.

From the Third Surgical Division, Bellevue Hospital.

3. For children from 6 to 12 years of age, three 5 grain tablets of prontylin are given three times a day (a total of 3 Gm.) and continued daily until the temperature has been normal for forty-eight hours.

4. Patients 12 years of age and over receive the following dosage:

First twenty-four hours, 100 grains (6.5 Gm.) of prontylin in divided doses.

Second twenty-four hours, 80 grains (5 Gm.) of prontylin in divided doses.

Third twenty-four hours, 60 grains (4 Gm.) of prontylin in divided doses.

Fourth twenty-four hours, 40 grains (2.6 Gm.) of prontylin in divided doses.

Small doses may be continued for two or three days after the temperature has reached normal, and the dosage may be subject to change at any time, depending on the condition of the patient. When any gastric distress resulted from the use of the drug, sodium bicarbonate in 10 grain (0.65 Gm.) doses was given with each dose of prontylin with excellent results. Antipyretics and magnesium sulfate should not be given in conjunction with prontylin or prontosil.

Prontosil was used in only a few adult cases at the beginning of the study. It was used as a routine in infants too young to take tablets and in those adults who were unable to take oral treatment. One 5 cc. ampule was given every four hours in adult cases. Infants received two 5 cc. injections a day.

From January 1 to July 1, 1937, 344 patients with erysipelas were treated by this method. These patients all received the same nursing care, the same dressings (boric acid solution or cottonseed oil) and the same diet. Cathartics were used freely, magnesium sulfate being avoided. Of the 344 patients treated in this manner thirty-one were children under 12 years of age, 219 were men and ninety-four were women.

The average hospitalization was 6.9 days for adults and 5.5 days for children. The total average was 6.8 days for all patients treated. On the fifth day 13.6 per cent of the patients left the hospital.

TABLE 2.—*Patients Treated with Erysipelas Antitoxin*

	Adults	Children
Cases treated	382	24
Days of hospitalization	11.1	12.8
Days of fever	6.8	10.0
Deaths	35	9
Mortality	9.2%	37.5%

TABLE 3.—*Patients Treated with Serum, Ultraviolet Rays, Roentgen Rays and Local Treatment with Dressings*

	Adults			
	Male	Female	Children	Total
Total cases	2,552	1,484	437	4,473
Average days' stay	11.26	11.09	10.77	11.11
Deaths	197	93	86	376
Mortality	7.7%	6.3%	19.7%	8.4%

The average number of days for the temperature to reach normal was 4.1 days for men, 4.4 days for women and 2.9 days for children. The total average was 4.1 days for all patients treated; 44 per cent reached a normal temperature on the third day.

Complications of erysipelas in adults treated with prontylin were as follows: spread of the lesion, three cases; abscess formation either at the site of the lesion or elsewhere, five cases; pustular folliculitis, two cases; acute infectious arthritis, two cases; pneumonia, one case, and cardiac arrhythmia, one case.

Certain reactions were observed and attributed to the drug: Twenty-seven patients became cyanotic, but this was not considered a contraindication, and usual dosage was continued. Nausea and dizziness were observed frequently and vomiting occurred in four women. In one patient slight jaundice developed which disappeared four days after medication was discontinued. This patient was a chronic alcoholic addict with an enlarged liver. Another patient who entered with a history and preexisting diagnosis of alcoholism and cirrhosis of the liver died with jaundice and cholemia during the course of the erysipelas and sulfanilamide medication. Autopsy was not permitted. In these two cases we did not attribute the cause of the jaundice to sulfanilamide. One patient showed slight hematuria. After injections of prontosil seven children showed a pink tinge to the skin due to the color of the dye (prontosil).

There were five deaths of adults, or 1.5 per cent, and four of children, or 12.9 per cent.

In an evaluation, this series (table 1) may be compared with 406 cases treated with erysipelas antitoxin during the winter of 1935-1936 (table 2).

The summaries of these tables may be compared with the results of 4,473 cases from Jan. 1, 1930, to Jan. 1, 1937, in which various methods of treatment were utilized—serum, ultraviolet rays, x-rays and local treatment with dressings of different kinds (table 3).

477 First Avenue.

THE PRODUCTION OF BREAST GROWTH IN THE HUMAN FEMALE

BY THE LOCAL APPLICATION OF ESTROGENIC OINTMENT

CYRIL M. MacBRYDE, M.D.

ST. LOUIS

The growth of the mammary glands in experimental animals has been extensively investigated and has been found to depend primarily on the estrogenic hormones.[1] Complete development in most mammals is dependent on the simultaneous action of estrogenic and corpus luteum hormones.[2] In spite of the excellent experimental background, I have been unable to find records of carefully controlled studies of human breast growth. I therefore performed studies on three women lacking mammary development and exhibiting signs of marked hypogonadism. In the first part of the study the hormones were administered by subcutaneous injection. I was able to demonstrate that, by the injection of from 150,000 to 350,000 international units of estrone or of estradiol benzoate per week, active mammary growth could be produced in patients who previously had no visible or palpable breast tissue. The results were recorded by frequent caliper measurements and photographs. During the treatment vaginal smears were changed from the inactive type to the active estrous state; there was enlargement of the

From the Department of Medicine, Washington University School of Medicine, and the Barnes Hospital.

1. Turner, C. W.: The Mammary Glands, Chapter XII, Sex and Internal Secretions, edited by Edgar Allen, Baltimore, Williams & Wilkins Company, 1932. Gardner, W. U., and Van Wagenen, G.: Experimental Development of the Mammary Gland of the Monkey, Endocrinology **22**: 164-172 (Feb.) 1938.

2. Turner, C. W., and Frank, A. H.: The Relation Between the Estrous Producing Hormone and a Corpus Luteum Extract in the Growth of the Mammary Glands, Science **73**: 295 (March 13) 1931.

uterus; the vagina became deeper and the vaginal walls, previously thin, smooth and atrophic, became rugated, thick and soft. There was considerable psychic improvement, the outlook changing from that of abnormal, almost asexual individuals to one approximating that of normal women. This was especially true after artificial menstrual periods had been produced one or more times. Hypogonadal symptoms such as hot flashes and emotional instability were relieved, the basal metabolism rose, the appetite improved and there was considerable weight gain in these previously very thin patients.

Although I was also able to produce breast growth with injections of ketohydroxyestrin (estrone), estradiol benzoate was, unit for unit, much more effective.

Corpus luteum extract, 5 international units daily for a period of thirty days, when given alone produced no detectable change in the breasts. This is in accord with the experimental observations on animals of Turner,[2] Corner [3] and others. When, however, patients were given alternate daily injections of 1 international unit of progesterone and from 20,000 to 50,000 international units of estrone or of estradiol benzoate, breast growth was more rapid than that produced by the estrogenic hormones alone. The simultaneous use of the corpus luteum and estrogenic therapy definitely produced a much firmer breast growth, which was distinctly lobular to palpation, whereas the growth produced by the estrogenic hormones alone was smooth and the borders of the glandular tissue were difficult to define. Rapid regression in the size of the breasts followed the omission of the hormone injections, but the regression was less rapid when the combined therapy had been used.

TABLE 1.—*Breast Growth Produced with Estradiol Benzoate Injections (Case 1)*

Date	Therapy		Breast Measurements (in Centimeters) Horizontal	Vertical	Depth	Areola
1/ 8/36	.....		No breast tissue			
	50,000 i. u. daily					
1/23/36	.....	R.	5.4	5.4	2.0	1.6
		L.	5.3	5.4	2.1	1.7
	50,000 i. u. daily					
2/ 1/36	.....	R.	6.0	6.0	2.4	1.9
		L.	6.1	6.0	2.3	1.9
	50,000 i. u. 3 times weekly					
2/21/36	.....	R.	6.0	5.9	2.4	2.0
		L.	6.0	5.8	2.4	1.8
	No treatment					
3/ 5/36	.....	R.	5.0	5.2	2.0	1.6
		L.	5.1	5.0	2.1	1.8
	50,000 i. u. 3 times weekly					
4/21/36	.....	R.	7.5	7.0	3.5	2.5
		L.	7.8	7.0	3.5	2.5
	50,000 i. u. daily					
5/13/36	.....	R.	8.8	8.0	4.2	2.5
		L.	9.0	8.1	4.2	2.6
	30,000 to 350,000 i. u. per week					
7/24/37	.....	R.	11.5	10.5	5.4	3.2
		L.	11.7	10.8	5.6	3.3

So far as was possible by clinical criteria alone, I was thus able to confirm in the human female what had been suggested by previous studies on breast growth of experimental animals. Table 1 includes some of these results, and the details of the studies are given in the case reports.

The second part of the investigation concerned the production of human breast growth by local inunction with estrogenic ointments. In the literature there is considerable evidence that estrogen is well absorbed through the skin and mucous membranes. The application of estrogens to the vaginal mucosa of animals has been demonstrated as more effective than injections in producing typical vaginal estrous changes.[4] The treatment of gonorrheal vaginitis in children, which is based on the vaginal changes produced by estrogenic hormones, is best accomplished by the use of vaginal suppositories containing the active material.[5] Excellent results in the treatment of pruritus vulvae and kraurosis vulvae have been reported with local estrogenic therapy.[6] Certain dermatoses associated with hypogonadism are said to respond to local hormone treatment.[7] Kun [8] demonstrated that, in rats, percutaneous estrogen acts locally to improve cutaneous nutrition and stimulate hair growth. Burrows, Ito and Moore [9] have shown that enough estrogenic material can be absorbed through the intact skin of animals to elicit the characteristic general effects of the hormone, including estrus and breast growth. When an ointment containing estrogen is applied to the breast region of guinea pigs, nipple growth is produced, and, when the application is unilateral, nipple growth is greater on the treated side.[10] DeFremery [11] found that treatment of virgin goats with pituitary lactogenic hormone caused

TABLE 2.—*Breast Growth Produced by Local Application of Estrogenic Ointment (Case 1)*

Date	Therapy		Breast Measurements (in Centimeters) Horizontal	Vertical	Depth	Areola
5/13/38	Size after omission of treatment	R.	4.8	4.8	2.0	1.6
		L.	4.8	4.8	2.1	1.7
	Left breast treated; right breast control					
5/28/38	.....	R.	5.4	5.4	2.1	2.0
		L.	7.0	7.0	3.1	2.5
	Left breast treated; right breast control					
6/ 8/38	.....	R.	5.4	5.4	2.7	2.0
		L.	8.2	8.2	4.0	2.8
	Right breast treated; left breast control					
6/17/38	.....	R.	7.2	7.0	3.3	2.9
		L.	8.2	8.2	4.0	2.9
	Both breasts treated					
7/17/38	.....	R.	11.8	10.8	5.3	3.1
		L.	11.8	10.7	5.6	3.1

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4. Loewe, S., and Voss, E. H. V.: Eine placentare Inkretdrüse Spenderin örtliche wirksamen Hormons? Klin. Wchnschr. **5:** 1083-1085 (June 11) 1926. Powers, H. H.; Varley, J. R., and Morrell, J. A.: Preliminary Note on Assay of Follicular Hormone by Vaginal Administration, Endocrinology **13:** 395-398 (July-Aug.) 1929. Berger, M.: Besonders hohe Wirksamkeit des Follikelhormons bei vaginaler Instillation, Klin. Wchnschr. **14:** 1601-1602 (Nov. 9) 1935.

5. Te Linde, R. W., and Brawner, J. N., Jr.: Experiences with Amniotin in the Treatment of Gonococcal Vaginitis in Children, Am. J. Obst. & Gynec. **30:** 512-523 (Oct.) 1935. Lewis, R. M., and Adler, E. L.: Endocrine Treatment of Vaginitis of Children, and of Women After Menopause, J. A. M. A. **109:** 1873-1875 (Dec. 4) 1937.

6. Tscherne, E.: Ueber den histologisches Nachweis der Wirkung perkutan zugeführten Follikelhormons bei der Kraurosis Vulvae, Zentralbl. f. Gynäk. **62:** 169-172 (Jan. 15) 1938. Jaffe, K.: Percutane Behandlung von Dermatosen mit Follikelhormon, Schweiz. med. Wchnschr. **67:** 477-478 (May 22) 1937. Klaften, E.: Zur Behandlung des Pruritus vulvae und bestimmter Formen von Dermatitiden, Zentralbl. f. Gynäk. **61:** 972-981 (April 24) 1937.

7. Jaffe.[6] Klaften.[6]

8. Kun, H.: Wirkungen der Follikelhormons auf die Haut bei perkutaner Verabreichung, Wien. klin. Wchnschr. **50:** 408-411 (March 26) 1937.

9. Burrows, H.: On Some Effects Produced by Applying Oestrin to the Skin of Mice, Am. J. Cancer **20:** 48-57 (Jan.) 1934. Ito, M.; Hajazu, S., and Kon, T.: Die percutane Wirkung der Sexualhormone, Zentralbl. f. Gynäk. **61:** 1094-1098 (May 8) 1937. Moore, C. R.; Lamar, J. K., and Beck, Naomi: Cutaneous Absorption of Sex Hormones, J. A. M. A. **111:** 11-14 (July 2) 1938.

10. Jadassohn, W.; Uehlinger, E., and Zuercher, W.: Zur Vergrösserung der Meerschweinchenbrustwartze durch Hormone; der "lokale Folliculineffekt," Klin. Wchnschr. **16:** 313-314 (Feb. 27) 1937. Mussio-Fournier, J.; Albrieux, A., and Buno, W.: Action locale de la folliculine sur la mamelle du cobaye male, Bull. Acad. de méd., Paris **117:** 64-66 (Jan. 12) 1937.

11. DeFremery, P.: On the Influence of Different Hormones on Lactation, J. Physiol. **87:** 50-51 P (May 16) 1936.

the secretion of only a few drops of milk. If, however, the udder was first treated with inunctions of estradiol benzoate there was considerable mammary development with changes of the preparturient type. Injections of lactogenic hormone at this stage induced lactation which was as abundant as that observed after parturition.

Loeser and Salmon [12] each found that the symptoms of castrate women could be relieved by percutaneous estrogenic therapy, and the latter demonstrated that a total cutaneous dose of from 160,000 to 300,000 rat units given over a period of from three to four weeks was necessary to produce a full estrogenic effect as determined by vaginal smears.

No studies have as yet appeared on the local effect of estrogen when applied directly to the human breast. I therefore omitted the injection therapy in my patients until the major part of the artificially produced growth had disappeared. An ointment of hydrous wool fat and petrolatum containing 5,000 international units per gram of estradiol or of estradiol benzoate was then applied directly to the breast region over a circular area approximately 10 cm. in diameter, with the nipple as the center. Each day 5 Gm., containing 25,000 international units, was applied, by the patient, to the breast region on one side, rubbed in for five minutes, and allowed to remain on over night. The breast of the other side was used as a control and received the same amount of ointment base, without the estrogen, and the same amount of massage.

Definite breast growth of considerable degree was produced by the estrogenic substance absorbed through the skin directly into the breast tissue. Evidence of absorption of the estrogen into the systemic circulation was found in the change of the vaginal smears from the inactive type to the active estrous state, by change in the vaginal mucosa, by enlargement of the uterus, by relief of the patients' hypogonadal symptoms and by slight effects on the opposite breast.

I found little or no difference in the effectiveness of the estradiol and estradiol benzoate ointments.

The ointments, unit for unit, were more effective in producing breast growth than injections of estradiol benzoate or of ketohydroxyestrin (estrone). Ointments containing estrone were less effective, unit for unit, than those containing estradiol.

When breast growth was produced by injections of estrogenic material, there was diminishing effectiveness of the injected hormones. When the hormones were applied to the skin, however, there was a steady progressive growth.

Caliper measurements were made at frequent intervals and a photographic record was kept of the changes produced. The accompanying tables and photographs are abstracted from these records at salient points in the studies.[13]

REPORT OF CASES

CASE 1.—An unmarried woman aged 24, first seen Dec. 3, 1935, complaining of lack of development of sex characteristics, nervous instability and hot flashes, had never menstruated. Many kinds of glandular treatment had been tried without success. Small doses of estrogen by injection had perhaps relieved slightly the subjective symptoms.

She was 5 feet 8¾ inches (175 cm.) tall and very thin, weighing only 111 pounds (50 Kg.). The arms and legs were long in proportion to the length of the trunk. From soles to symphysis pubis she measured 37¼ inches, from symphysis pubis to vertex 31½ inches. The span with the arms outspread exceeded her height by 4½ inches. The face and manner were very feminine but there was no sign of breast tissue, the hips were narrow, the external genitalia and vagina were infantile and the uterus could not be palpated. Hair growth was normal except that it was very scanty in the pubic region. The skin was smooth, clear and delicate. Laboratory studies were within normal limits, except for the following: the basal metabolism was minus 15 per cent, the sugar tolerance curve was flat; roentgenograms showed that epiphysial union had been delayed and had not yet occurred in the phalanges or at the distal end of the radius and ulna, and the vaginal smears were of the inactive or "castrate" type.

Substitution therapy with large doses of estrogenic hormone was advised. It was thought that the patient's ovaries were either absent or so atrophic that little or no effect could be expected with pituitary gonadotropic substance.

Treatment was started Jan. 8, 1936, with daily subcutaneous doses of 50,000 international units of estradiol benzoate. Within

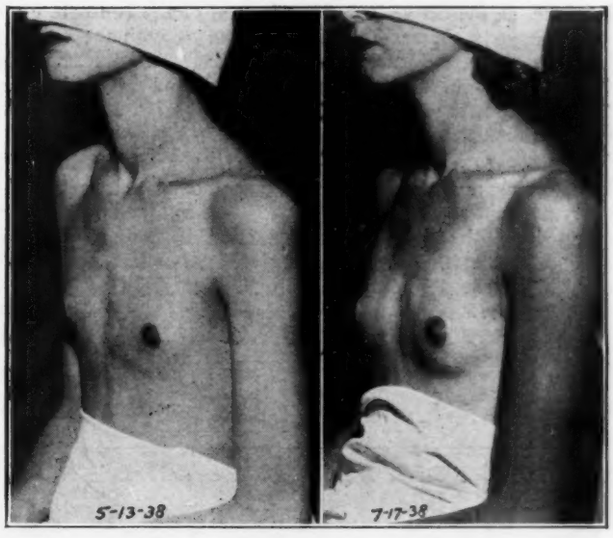

Fig. 1 (case 1).—Breast growth produced after eight weeks' application of ointment to the mammary region.

twelve hours after the first injection the patient noticed a clear vaginal secretion, never before present. There were also some lower abdominal pains which suggested uterine cramps. These results became more definite after the second injection. After six injections there was tenderness and enlargement of the nipples and areolae, and a darkening in color of the latter. At this time a disk of firm tissue about 4.5 cm. in diameter was noted under each areola. The labia were very sensitive. After ten injections the breasts measured 4.7 cm. in diameter and the uterus was palpable for the first time. The vaginal walls were turgid and rugated. February 1, after twenty-four daily injections, the breasts were 6.0 cm. in diameter and 2.4 cm. deep and the uterus was larger, although still much smaller than normal. At this time the dose was diminished to 50,000 international units three times weekly. The breast growth was maintained with this dose but did not increase during the next three weeks. All treatment was stopped for a control period of two weeks and there was rapid regression in the size of the breasts. Four days after cessation of treatment rather profuse vaginal bleeding occurred, lasting six days. The psychic effect of this was considerable. The patient said that now she had menstruated for the first time she felt like a normal woman. Treatment was resumed with 50,000 international units three times weekly and there was slow growth. Resumption of 50,000 international units daily brought a rapid increase in size of the breasts, nipples and areolae. During the next thirteen months the patient received from 30,000 to 350,000 international units a week. Definite breast regression occurred with less

12. Loeser, A. A.: Resorption and Action of Follicular Hormone Rubbed Into the Skin, J. Obst. & Gynaec. Brit. Emp. **44**: 710-714 (Aug.) 1937. Salmon, V. J.: Skin Absorption of Dihydroxyestrin in Humans, Proc. Soc. Exper. Biol. & Med. **38**: 481-484 (May) 1938.

13. Estradiol benzoate (progynon B), corpus luteum hormone (proluton) and estrogenic ointments were supplied for these studies by Dr. Max Gilbert and Dr. Gregory Stragnell of the Schering Corporation. Estrone (amniotin) was supplied through Dr. J. A. Morrell of E. R. Squibb and Sons.

than 100,000 international units a week. A maximum point of growth was attained with 350,000 international units a week. Continuation of this dosage accomplished no further increase in the breast size. Table 1 shows the breast measurements at various stages of the treatment. On estrogen therapy alone the patient gained weight from 111 to 130 pounds (50 to 59 Kg.) and the basal metabolic rate rose from minus 15 to plus 4 per cent.

All treatment was omitted for a period of thirty days. The left breast only was then treated daily with 5 Gm. of the ointment containing 25,000 international units of estradiol benzoate. The right breast was treated with the ointment base without the estrogen. The left breast increased in size while the right one showed little change. This was evident in ten days, and the unilateral treatment and growth continued for twenty-three days. Treatment of the right breast alone brought them to equal size; then bilateral treatment was given for twenty-eight days. The skin received a total dose of 50,000 international units daily. The rate of growth and total growth produced by this dose to the skin were slightly in excess of that produced by subcutaneous injections of 50,000 international units daily (table 2). Omission of the ointment treatment was followed by vaginal bleeding and rapid regression in breast size. The ointment treatment was then resumed with estradiol, the free hormone, as the active ingredient instead of the benzoate ester. Approximately the same results followed as with the estradiol benzoate ointment. Table 2 shows the breast measurements at various stages of the ointment treatment and figure 1 shows the patient before and after the treatment of the breast with estrogen inunctions.

CASE 2.—An unmarried woman aged 24, first seen March 8, 1938, complained of lack of development of sex characteristics, anorexia, underweight and nervousness. She had never menstruated. With desiccated thyroid one-half grain (0.03 Gm.) once daily and theelin 10,000 international units once weekly she had improved slightly. The basal metabolic rate had risen from minus 15 per cent to plus 1 and she had gained a little weight. There had never been any breast development, either before or after the injections.

She was 60 inches (152 cm.) tall and weighed 89½ pounds (40.6 Kg.). She had the general appearance of a girl of

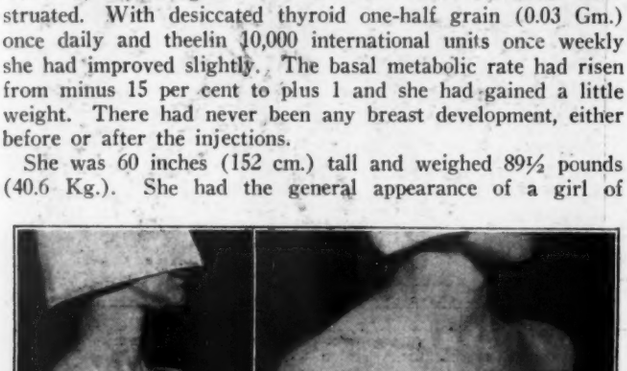

Fig. 2 (case 2).—Breast growth produced after three and one-half months' use of estrogenic ointment.

approximately 12 years. The manner was entirely feminine, the hair and skin were normal. There was no visible or palpable breast tissue. The areolae were very small. Their color was that of the surrounding skin. The very small nipples were inverted. The external genitalia and vagina were infantile and the uterus was impalpable by rectal examination. Vaginal smears were of the inactive type.

Treatment was started with 100,000 international units of estradiol benzoate subcutaneously three times weekly. The first notable effect was the appearance of a vaginal secretion at the end of forty-eight hours. After ninety-six hours (two injections) there were abdominal cramps, presumably uterine, and the vaginal smears showed active estrous changes. The nipples became erect and the areolae larger and darker by the end of the first week's treatment. The labia minora and majora enlarged, and after three weeks of treatment a small uterus was palpable by rectum. A disk of breast tissue was palpable at the end of the first week, and there was progressive breast growth at approximately the same rate as that obtained in

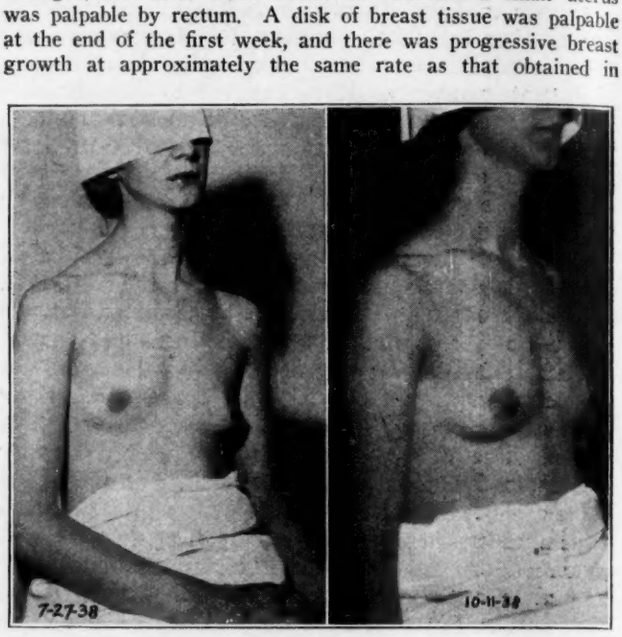

Fig. 3 (case 3).—Breast growth produced after treatment only of right breast for twelve weeks with ointment.

case 1. When the estrogen injections were omitted, vaginal bleeding occurred for the first time in the patient's life and lasted four days. Breast growth regressed on omission of therapy but was resumed when injections were resumed. After three months of treatment the breast diameters were approximately 10.5 by 8.0 cm., their depths 4.5 cm.; the areolae measured 2.8 cm. Treatment with 50,000 international units daily except Sundays (300,000 international units a week) was continued and no further increase in breast size occurred. Treatment was then omitted for two weeks and the breasts became smaller, the diameters being approximately 6.1 by 5.8 cm. and depths 2.5 cm.

TABLE 3.—*Breast Growth Produced by Local Applications of Estrogenic Ointment 25,000 International Units Daily to Right Breast Only (Case 3)*

Date		Breast Measurements (in Centimeters) Horizontal	Vertical	Depth	Areola
7/27/38.....	R.	5.0	5.0	2.5	1.6
	L.	6.8	6.6	3.7	2.9
8/ 5/38.....	R.	5.8	5.8	2.9	2.1
	L.	6.8	6.8	3.9	2.9
9/ 8/38.....	R.	7.8	7.5	4.0	2.5
	L.	7.5	7.2	4.1	2.6
10/19/38.....	R.	9.8	9.5	5.8	3.2
	L.	8.5	8.3	4.8	2.9

Estradiol benzoate ointment was then applied to the right breast only, and the left breast was used as a control, receiving the ointment base without the estrogen. The right breast definitely increased in size during a two week's period, while the left gland showed little change. The ointment was changed to estradiol, the unesterified form, and growth continued at the same rate. After nine weeks' treatment the right breast measured 9.8 by 9.0 cm., depth 4.4 cm., areolae 2.5 cm.; the left breast measured 7.1 by 7.0 cm., depth 3.5 cm., areola 2.2 cm. The left breast was then brought up to the size of the right by treating it alone for three weeks. Then both breasts were treated, each receiving 25,000 international units of the estradiol ointment, a total of 50,000 international units daily to the skin. After five weeks of the bilateral treatment

each breast measured approximately 10.4 by 10.3 cm., depth 5.1 cm., areola 2.7 cm. and the areolae were large and dark, nipples large and erect. Figure 2 shows this patient before and after the ointment therapy.

CASE 3.—A married woman aged 28 complained of nervousness, long periods of amenorrhea and breast atrophy. Her breasts and menses had been approximately normal until after the birth of a child. Thereafter her periods were scanty, were of very short duration, and occurred at intervals of from six to twelve weeks. Both breasts had become very small but the right one had atrophied to such an extent that it was only half the size of the left. Vaginal smears showed variations from slight to moderate estrous activity. The vagina was normal, the uterus small.

Ketohydroxyestrin injections were started in doses of 30,000 international units three times weekly. Slight breast growth on both sides resulted, but after six weeks of this therapy a level was reached beyond which no further growth was evident. The right breast remained much smaller than the left. Ketohydroxyestrin 50,000 international units three times a week was given and there was some increase in breast size with the larger dosage. All treatment was then omitted. It was thought that this patient, whose right breast was considerably smaller than the left, presented an excellent opportunity for study of the local ointment effect. The breasts became much smaller after the injections were discontinued for twenty-six days.

Beginning July 27, 1938, 5 Gm. of the estradiol ointment containing 25,000 international units was applied to the right breast daily. The left breast received the control treatment with hydrous wool fat-petroleum ointment base without the estrogen. There was a gradual increase in the measurements of the right breast until after twelve weeks' treatment. October 19 the right breast actually was larger than the left (table 3, fig. 3). Systemic absorption was manifested by relief of nervousness, marked increase in vaginal secretion, enlargement of the uterus, the constant presence of vaginal smears showing marked estrous activity, and some increase in the size of the left breast.

COMMENT

These studies demonstrate that estrogens can be absorbed through the skin of the human female directly into the breast tissue and by this route can produce their characteristic stimulation of mammary growth. It is definitely not recommended that this method be adopted in general practice until further studies can be done and the limitations and possible dangers of the cutaneous application of concentrated estrogens can be defined.

From the strictly histogenic standpoint, the mammary glands should be considered as appendages of the skin and may be regarded as modified sweat glands. The glandular elements of the breasts are derived from the ectoderm. When local action of administered hormones is desired, it seems as logical to use the percutaneous treatment to the breasts as to use estrogenic substances on the vulva and in the vagina to relieve kraurosis or vaginitis. For the many patients in whom only a general effect is desired, the method of choice will no doubt continue to be subcutaneous or intramuscular injection. As we learn more about the local action of hormones, however, it may be necessary to choose between routes which involve the entrance of hormones into the general circulation and those which depend on local action on organs or tissues accessible from the exterior.

CONCLUSIONS

Estrogenic hormones applied to the skin of the mammary region of the human female will act locally to produce breast growth. Systemic effects such as are obtained by the injection of large doses of estrogen were produced by percutaneous absorption of the administered hormones.

600 South Kingshighway.

Clinical Notes, Suggestions and New Instruments

GLOMUS TUMOR (GLOMANGIOMA)

CLARMONT PAUL DOANE, M.D., FRESNO, CALIF.

Glomus tumors of the digits of the upper extremities have been recognized since they were first described by Masson [1] and Barré and Masson [2] in the French literature in 1924. These tumors are comparatively rare and are probably frequently overlooked clinically. Bailey [3] reports that in the eleven years following Masson's description of the tumor only fifty-eight instances of glomus tumor were recorded. If they are not overlooked, their exact nature may not be clear. It is my purpose in this report to call attention to them briefly and to record a typical case.

Glomus tumors may occur anywhere over the cutaneous surface of the body, but they occur most frequently in the extremities,[3] and especially in the digits of the upper extremities. The histologic structure is now well known, and the histogenesis of the glomus tumor was readily established.[4] Those interested in the histology of the tumors are referred to Bailey's [3] detailed report.

Fig. 1.—Section from specimen obtained in case reported. Note irregular vascular lumens surrounded by glomus cells. The vessels are separated from one another by homogeneous material. Reduced from a photomicrograph under low power.

The tumor is solitary and small and is a rose or purplish blue. It varies in diameter from 4 mm. to 10 mm.[5] The tumor may be raised so that it is easily seen, or it may extend into the subcutaneous tissues and be neither visible nor palpable.[6] These tumors are exquisitely tender, and pressure on one produces lancinating pain of a severe variety. External cold may produce paroxysms of pain. It is described as a burning, stabbing pain, which radiates up the extremity (if the tumor occurs in a digit). Cases have been reported in which these

1. Masson, Paul: Lyon chir. **24**: 257 (May-June) 1924.
2. Barré, J. A., and Masson, P.: Bull. Soc. franç. de dermat. et syph. (Réunion de Strasbourg) **31**: 148, 1924.
3. Bailey, O. T.: Am. J. Path. **11**: 915 (Nov.) 1935.
4. Masson.[1] Barré and Masson.[2] Bailey.[3]
5. Christopher, Frederick: Textbook of Surgery, ed. 3, Phlaidelphia, W. B. Saunders Company, 1936, p. 150.
6. Kolodny, Anatole: Ann. Surg. **107**: 128 (Jan.) 1938.

painful tumors have been present for as long as thirty years. Kolodny [6] in a recent report calls attention to a case in which sweating of the finger on irritation of the nodule was noticed. He feels that this phenomenon adds to our knowledge concerning the physiology of sweating.

In four of Adair's [7] cases the tumor was associated with the bed of the nail. Masson's patients had subungual tumors, My case is that of a subungual tumor.

REPORT OF CASE

Mrs. D. R. C., aged 31, white, a housewife, was referred to me by Dr. R. J. van Wagenen March 8, 1938. For years she had suffered from pain in the tip of the middle finger of her

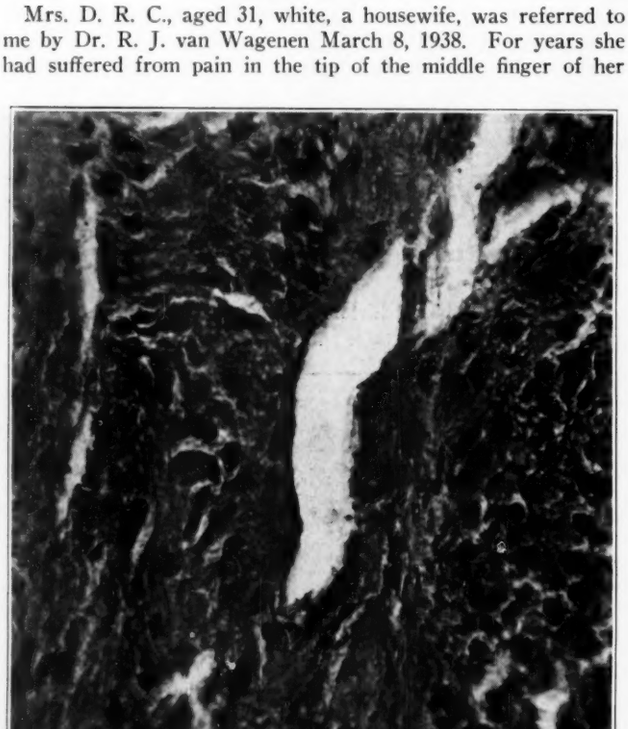

Fig. 2.—Showing the numerous, irregular vessels and clusters of glomus cells. Reduced from a photomicrograph under high power.

left hand. She could not remember when she first began to have this pain, but she associated its onset with a severe contusion of the ring finger of the same hand when she was about 10 years old. The middle finger was not involved in this accident. For a year or two after she first began to notice it the pain gradually became worse and the tip of her finger became more sensitive. During the next eighteen years there was little change in the character of the pain or of the tenderness. She was observed occasionally by various physicians, who offered no treatment that gave her relief.

About two years ago she began to notice an increase in the tenderness and in the amount of pain that she experienced. Whereas formerly radiating pain was not severe, it now became quite marked. At times pain, which originated in the tip of her finger, radiated well up into the arm and was of an intense nature. Thinking she was suffering from some inflammatory lesion, and on the advice of a physician, she had roentgenograms made of the painful digit. The roentgenograms were reported negative. About this time amputation of the finger was advised as being the only solution for her problem.

For two years she postponed doing anything about the proposed treatment, hoping that her finger would eventually cease to be painful. Recently, however, the pain became so bad that "all (her) fingers ache," and she was becoming desperate enough to submit to any treatment which could offer her relief.

7. Adair, F. E.: Am. J. Surg. **25**: 1-6 (July) 1934.

Examination of the finger revealed that it looked normal, apparently no different from any of the other fingers. The patient localized the source of the pain in a small area beneath the nail, at the margin of the lunula. She insisted that she could notice a "bluish" discoloration at the point which, when touched, gave rise to the pain. When the finger was observed in direct sunlight an area could be seen which seemed to have a slightly deeper color than the rest of the nail bed. The difference in shade was so slight as to make one wonder whether it was actually present. Pressure over this area gave rise to pain which was almost intolerable. No other areas of abnormal sensation were found on this or any of the other fingers.

A diagnosis of subungual glomangioma was made, and removal was advised. A tourniquet was applied, and under local anesthesia the nail was removed. The matrix was incised over the point of tenderness noted previously. When the matrix was spread, a mass of what appeared to be fat tissue protruded. A small, soft, encapsulated tumor about 5 mm. in diameter was removed. The tumor resembled a small lipoma. The bed of the tumor was smooth and extended inward to the terminal phalanx. Hemorrhage from the tumor bed, after release of the tourniquet, was quite profuse but was readily controlled by the application of pressure for a few minutes.

The specimen obtained was submitted for pathologic examination, and the pathologist's report confirmed the clinical diagnosis of glomangioma.

Convalescence was uneventful. The patient experienced none of the former pain. Two months after surgery the nail had grown normally and was nearly as long as the other nails. There was no tenderness, and the patient was completely free from pain.

SUMMARY

Glomangiomas, though rare, are worthy of attention because when they do occur they are extremely painful and quite disabling. As in the case presented, the true nature of the condition may be overlooked clinically.

510 San Joaquin Light and Power Building.

CONGENITAL ABSENCE OF BONES OF THE LOWER LIMB

JAMES A. BRUSSEL, M.D., BRENTWOOD, L. I., N. Y.

While anomalous conditions, present at birth, of the bones of the leg and foreleg are not rare, they are sufficiently unusual to be reported and should be recorded to maintain accurate statistics in these cases. Unfortunately, the figures of the early eras, particularly those prior to use of the roentgenogram, have been inaccurate chiefly because of the paucity of clinical means to ascertain definite pathologic conditions and, as a result, some of these observations have since been revised. For example, in 1846 Proudfoot (quoted by Cotton and Chute)

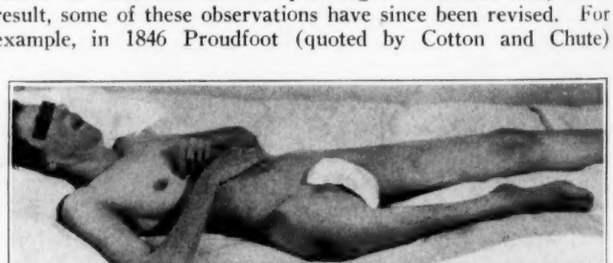

Fig. 1.—Patient in supine position after narcotization administered because she would not cooperate in conscious state. The deformed limb appears bent at the knee but is perfectly straight, outstretched and parallel to the normal left leg.

reported a case of congenital absence of the fibula in which he stated that ". . . the tibia of the same limb seemed to have a compound fracture at the middle. . . ."

Freund [1] regards the figures of Nilsonne [2] as the most conservative in the review of congenital absence of the femur.

From the Female Reception Service of the Pilgrim State Hospital.

1. Freund, Ernst: Congenital Defects of Femur, Fibula and Tibia, Arch. Surg. **33**: 349-391 (Sept.) 1936.

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The latter collected seventy-two cases up to 1928 and added ten of his own. Since then the literature has disclosed twenty-one additional cases,[3] which, with the one about to be reported, represent a total of 104 cases. This number is to be regarded as small for a period of almost a century. Dankmeijier[4] uncovered seventy-seven cases of congenital absence of the tibia of which twenty-one were bilateral, up to 1935, and added one case of his own. Since then sixteen others have appeared,[5] bringing the total up to ninety-four. For the fibula, Nutt[6] reduced Handek's[7] figure to ninety-eight, and since then sixteen more have been added,[8] bringing the total to 114.

To recapitulate, congenital absence of the bones of the lower limb reveals the following totals: (*a*) femur 104, (*b*) tibia ninety-four and (*c*) fibula 114.

The etiology of the absence of a bone or bones at birth has not been definitely established, though several interesting ideas have been suggested. Most writers have discarded the "primitive fin theory," advanced by Gegenbauer, and lean to the amniotic theory as probably more correct. Cotton and Chute have explained the lesion on this basis, as have Tubby, Taylor and others. As early as 1910, Whitman[9] felt that the deformity is associated with absence of bone due either to an original defect in the germ or to interference with its development. However, he did believe that amniotic adhesions might be one of the predisposing causes. Reiner states that the first cause of the condition is due to external pressure on the embryo from the amniotic bands, and the second a faulty development of the embryonic tissue and cartilage. More recently, Ollerenshaw[10] has written that the predominant cause is undoubtedly a cessation of growth in one or the other set of embryonic cells at a period he places between the fourth and the sixth week of fetal life.

The psychologic implication of such a condition becomes quite apparent, especially when a frank psychosis develops in a person born with this defect which might, on first glance, be attributed to the birth defect. The report of such a case follows:

History.—H. F., a white woman aged 34, married, was native born of Irish descent.

The family history was negative for mental or nervous diseases for at least two generations.

The patient was the ninth child in a family of eleven, born in Pennsylvania July 14, 1903. The congenital absence of the right femur was noted at birth but never created a great disability, since the patient learned to get about quite well with a crutch, nor did she ever openly express any inferiority because of this infirmity. She completed two years of high school education by the time she was 15 and following this worked as a typist and telephone operator without experiencing any difficulty. Otherwise her medical and surgical history is negative. She married at the age of 24; she has one child but no other pregnancies. She is described as having been friendly, sociable, alert, active and particularly fond of music. While her husband states that marital life has been quite satisfactory, a sister of the patient insists that this is not true and that many quarrels have taken place at the home and on one occasion the husband left the patient.

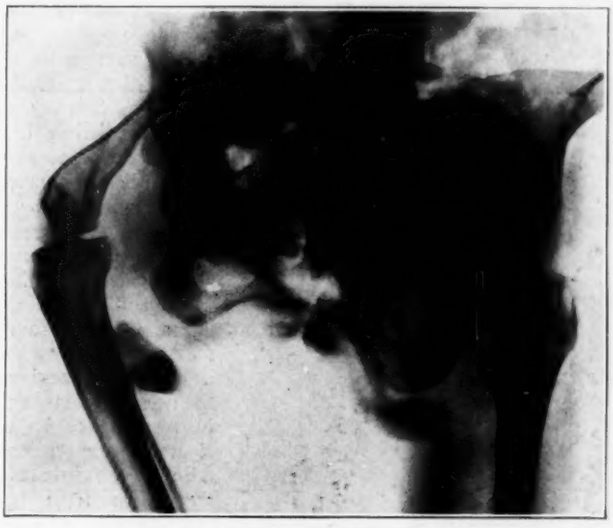

Fig. 2.—Appearance of the hips. The right limb shows rudimentary remains of an immature lower end of the femur.

Psychosis.—The patient's sister feels that the psychosis is the culmination of a long series of marital difficulties, while the husband associates it with the death of the patient's mother in November 1936. Shortly after this death the patient began to pray a great deal, showed little interest in what went on about her and finally began to refuse food. She was not very communicative but finally expressed a fear that her husband and others were trying to poison her. Her actions became increasingly strange and bizarre. She would open doors and peer out as if looking for some one or something but never expressed her thoughts freely in words. She finally became mute and withdrawn; she would lie on her bed totally inactive but would eat if food was left in her room and she was entirely alone. Jan. 22, 1937, she was admitted to the psychopathic ward of Bellevue Hospital, where physical examination corroborated the foregoing observations. Mentally she was mute, negativistic and passively resistive.

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Ke Ping Jen: Congenital Defects of Tibia, Arch. f. orthop. u. Unfall-Chir. **37:** 42-47, 1936.

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She was admitted to Pilgrim State Hospital January 29 on a regular order of commitment. During the admission routine she was entirely mute. Physical examination revealed malnutrition, an asthenic habitus and absence of the right femur, subsequently corroborated by roentgenographic studies. The roentgenograms (figs. 2 and 3) show that the head of the tibia is attached to a rudimentary union of approximately the lower eighth of what would have been a femur, but even the lower end of this femur shows poorly demarked condylar processes. Figure 1 was taken of the patient in the supine position after she had been narcotized with sodium amytal, since she would not cooperate for a photograph in her conscious state. The deformed leg appears as a bent knee, but this is not the fact. The leg is in its normal outstretched position and parallel to the normal leg. There were retroversion of the uterus and lacerations of the cervix. The Wassermann reaction of the blood and routine laboratory examinations were all negative. Mentally the patient was passively resistive, kept her eyes closed, was entirely mute and showed no emotional display of any sort. She lay on the examining bed with a blank expression on her face, occasionally relieved by a weak smile. The musculature was relaxed and atonic. She has subsequently remained essentially the same, though sometimes she is observed laughing to herself as though in response to hallucinatory experiences. She is completely withdrawn from her environment, showing little spontaneous interest or activity but seemingly preoccupied with her fantasies or hallucinations. Her condition was diagnosed as schizophrenia (dementia praecox), catatonic type.

Fig. 3.—Appearance of right hip showing "knee joint in right pelvis."

Regarding the psychologic implications in this case, adherents of Adler's theory of organic defect will find admirable substantiation of their belief, as is not unusual in any functional condition such as a catatonic state in which muscular and postural phenomena are noted. However, opponents to this idea will claim that the patient adjusted more than satisfactorily to the demands of society despite this defect and that only with the advent of an unhappy marriage did the psychosis develop, the unfavorable union being interpreted by the ego as a threat to its integrity with the need for withdrawal from reality for its preservation. Of course adlerians may argue that the patient felt that her failure at marriage was due to her deformity appearing as a disagreeable entity to her husband. While such arguments pro and con could continue ad infinitum, it is not my purpose in this paper to favor one side or the other. Suffice it to say that in this case the prognosis is definitely poor. Hypoglycemic shock therapy was not attempted because, at the time, insulin and/or metrazol therapy had not yet been employed in this country with the widespread use it is now accorded.

The Length of Life.—In the sixteenth century the average length of life in western Europe is said to have been nineteen years; in the seventeenth century, twenty-five years; in the eighteenth century, thirty-two years. In the nineteenth century in this country life averaged about forty years, but by the end of the first quarter of the twentieth century the life expectancy at birth had increased to about fifty-seven years for boys and to about sixty years for girls.—Diehl, Harold S.: Healthful Living, New York, Whittlesey House, 1935.

Special Clinical Article

THE OPHTHALMOSCOPIC SIGNS OF CONSTITUTIONAL DISEASE

A SUMMARY OF THE SALIENT POINTS MADE IN A LANTERN SLIDE DEMONSTRATION OF COLOR PHOTOGRAPHS OF LIVING HUMAN EYES

CLINICAL LECTURE AT SAN FRANCISCO SESSION

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ALBANY, N. Y.

The background of the eye is the stage on which many of the tragedies of life are enacted. By careful, repeated examination, early changes can be detected and steps taken to eradicate or diminish the ravages of destructive forces.

By the use of a simple ophthalmoscope and the expenditure of a little time and concentration every physician will be able to recognize the fundus signs of the major vascular changes and the alterations from diabetes, hypertension, nephritis, syphilis, tuberculosis, intracranial pressure and optic nerve inflammations.

Obviously, before any one attempts to diagnose fundus lesions he must be well grounded in the great number of physiologic variations. For that reason, a careful analysis must be made of every case, and a detailed, orderly inspection should be followed by a judicial review of the possibilities before one arrives at a prognosis.

The normal disk may be comparatively small or rather large. It is paler than the surrounding fundus and may be outlined with a white or pigmented arc or ring. In the center of the disk there is a depression which varies much in diameter and depth; this, the central excavation, is an important landmark.

The retinal vessels course over the disk and the entire visible fundus. The arteries are easily distinguished from the veins by their lighter color and rounder form. The number of branches and the method of distribution from straight to very tortuous are never the same, so that each fundus is a distinct entity. The dark region of the macula is usually two disk diameters beyond the temporal edge of the disk and slightly below the horizontal level. Overlying its deepest part is a bright spot, to which the name foveal reflex has been given. In reality the shining dot comes from the vitreous and not the retina. The color of the background may be a uniform pink or almost white, through which the choroidal channels are easily seen and distinguished from the regularly arranged pattern of the retinal tree, or it may be mottled, with dark and light markings.

Fig. 1.—A normal fundus. The bright figure eight is the image of the carbon arc which supplies the illumination. The pale oval center is the nerve head from which the vessels diverge. The dark region to the left is the macula. The veins are wide and darker than the arteries.

Read in the General Scientific Meetings at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 13, 1938.

During the course of embryologic life certain anomalies may develop. The border of the nerve head may fade into a pale arc or a depressed crescent, or, in the extreme case, the end of the optic nerve may lie in a cup of undeveloped choroid; the macular region may be an oval white hole, a coloboma, or a large portion of the choroid may be absent in the lower segment of the fundus. The sheath of Schwann may pass beyond the lamina cribrosa and appear as glistening white, small or large masses about the disk or in remote portions of the fundus. The teased, shredded, fibrillated structure is diagnostic and should never be confused with exudate. Bright glistening yellowish dots lying beneath the retinal vessels are called druse. They never interfere with vision and may be isolated or confluent even to the extent of forming a thick, dappled sheet.

When sufficiently trained every physician should be able to recognize pathologic signs. The correct interpretation of all of them is a life study, and yet every one can become proficient enough to recognize gross changes and by constant daily application steadily improve his diagnostic capacity.

The easiest way to begin the study of fundus diseases is by examination of the changes in the retinal blood vessels.

Sudden occlusion of the central retinal artery presents a characteristic appearance; the back of the fundus turns white. This is seen a few minutes after the patient complains of sudden blindness, which comes on unaccompanied by pain or congestion of the eyeball. The macula is dark red. After several days the pallor lessens, but the blindness persists. Eventually, if it was caused by an embolus one or more sclerotic patches form in the wall of the artery or arteries.

When the closure follows a chronic disease of the blood vessels the terminal shutting off of circulation produces a white zone similar to but sometimes less intense than that found in embolism. Retinal hemorrhages and white exudates are probably always present.

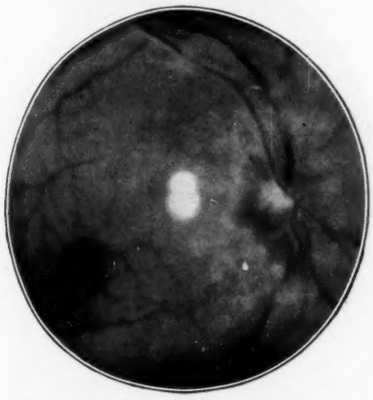


Fig. 2.—Embolism of the central retinal artery, right eye of a man aged 51 a few hours after sudden and complete blindness; white edema, pink nerve head and red macula.

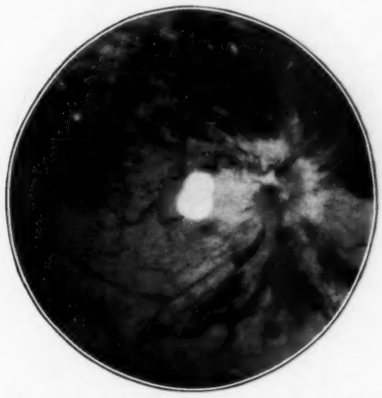


Fig. 3.—Thrombosis, endarteritis obliterans, of the central retinal vein, right eye of a man aged 48; blood distributed over and between the arcuate nerve fibers of the retina.

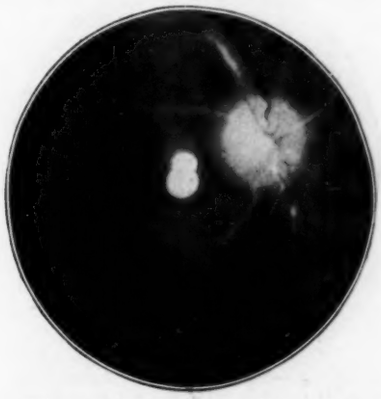


Fig. 4.—Arteriosclerosis, right eye of a man aged 51; narrow arteries with white sclerosed patches and visible walls.

Occlusion of an isolated artery branch may produce a localized whiteness corresponding to the region nourished by it. An oval central zone may receive its blood supply through the cilioretinal system, and in that way central vision is retained even when the major retinal artery is imperforate.

In sharp contrast to a closed artery is a plugged vein. When the central retinal vein is thrombosed the distal branches become immensely engorged, appearing as tortuous red loops which dip into the swollen retina and are lost to view. There are many hemorrhages and often white exudate flecks. Thin linear hemorrhages follow the course of the arcuately distributed retinal fibers. Closure of a branch may, when the blood seeps down and covers the macula, materially interfere with vision. The blood may absorb, leaving little or much residual damage, or there may be a sudden, sharp pain with congestion of the eyeball, a dilated pupil and an increase in intra-ocular tension, hemorrhagic glaucoma, which does not respond to treatment and almost invariably leads to enucleation.

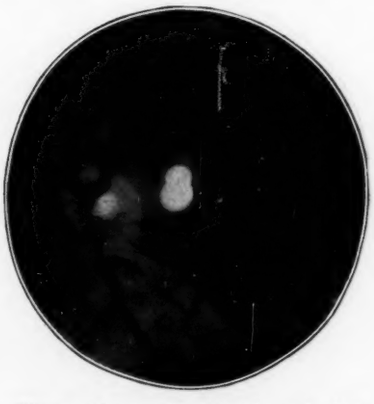


Fig. 5.—Hypertensive retinitis, early stage, left eye of a man aged 50; blood pressure 224/108, increased artery reflex, edema of retina, gray-white cloudy patches.

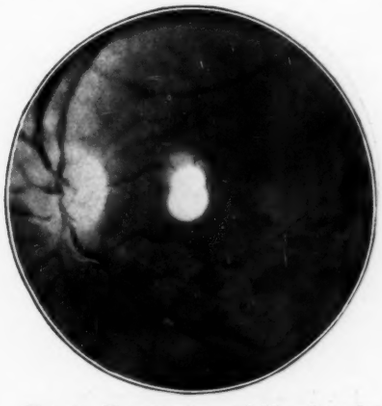


Fig. 6.—Hypertensive retinitis of twelve years' duration, left eye of a man aged 62; blood pressure 220/160, artery wall reflex increased, veins indented, many hemorrhages in the retina.

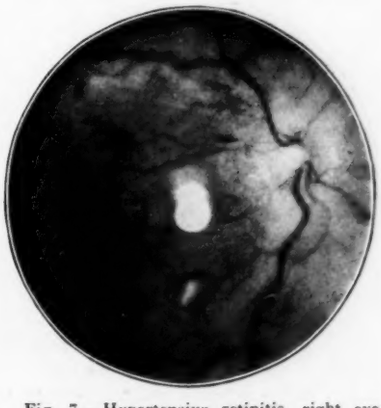


Fig. 7.—Hypertensive retinitis, right eye of a man aged 59, fourteen months before death; widespread retinal edema, irregular caliber arteries, many fresh and old retinal hemorrhages, blood pressure 182/100.

Gross retinal arteriosclerosis should be a common disease of the fundus, but actually it does not often reach the great white atherosclerotic stage. White patches in the artery may be observed through their advancing stages until occasionally the walls become white cords similar to the pipestem radials of far advanced general arteriosclerosis. Care must be taken not to confuse the increased visibility of vessels on or close to the disk as an indication of arteriosclerosis, for in this region the vessel sheath is often visible and yet devoid of pathologic significance. In syphilis white artery walls are not uncommon.

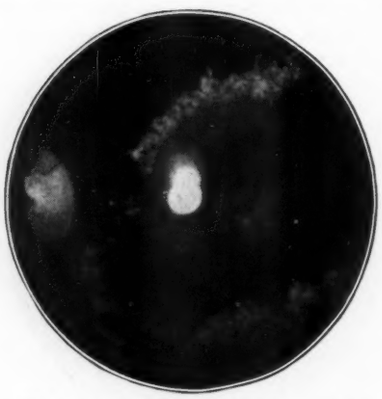


Fig. 8.—Senile macular degeneration, retinitis circinata type, left eye of a woman aged 72; a crown of whitish retinal exudates surrounds a gray edematous degenerating macular region.

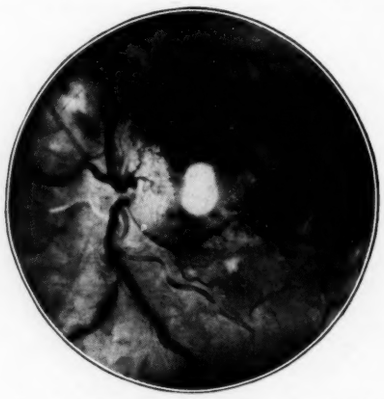


Fig. 9.—Malignant hypertension, nephrosclerosis, left eye of a man aged 44, who had had hyperpiesia for years and who died of uremia four weeks after photograph was taken; extreme artery changes, with sclerosis, irregular caliber and stiff walls indenting full veins, retinal edema and hemorrhages, new vessels on disk.

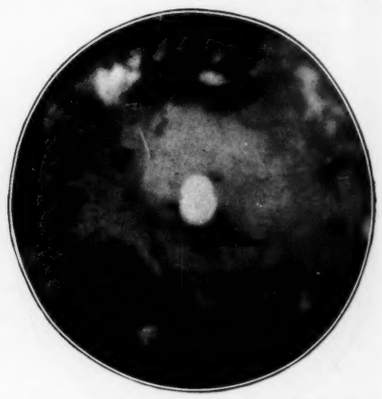


Fig. 10.—Nephritic neuroretinitis, left eye of a woman aged 23, fourteen months before death; great hemorrhages on the sides of the swollen nerve head, waxen exudate with suggestion of a star.

Arteriosclerosis and retinal hypertension are so often combined that the association deserves careful attention because of the increasing prominence it is receiving and will continue to merit. If the presence of edema is considered a requisite of hypertensive retinitis, then the characteristics of the disease can be defined as edema, greatest where the retina is thickest, usually the nasal side of the disk, and a few or many hemorrhages, combined with whitish, gray, soft masses usually near the major vessels. These signs will ultimately become more dominant with more hemorrhages, more and larger snowbank masses and greater nerve head swelling. If the patient does not die at this time, the edema, the hemorrhages and the exudates often subside until only a mere trace remains. Then or shortly thereafter dark chocolate brown spots appear near the posterior pole. These are of serious import and are one of the more certain signs of impending dissolution.

Fig. 11.—Renal retinitis, right eye of a man aged 33, who had had nephritis for three years and who died in coma three months later; gray retina, macular star exudate.

Fig. 12.—Retinitis in diabetes, left eye of a woman aged 62; blood sugar content 157 mg.; extensive, glistening, yellow-white exudates, many retinal hemorrhages.

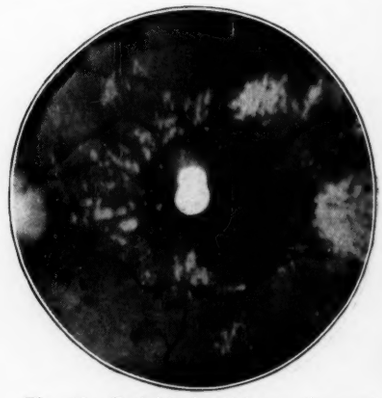


Fig. 13.—Retinitis in diabetes; the same case as that represented in figure 12, the photograph having been taken six months later; extension of retinal change even when the diabetes was seemingly under control.

While these fundus manifestations pass through their cycle (and, incidentally, this may take twenty or more years) the vessels have undergone the changes which make it practically impossible to distinguish sharply arteriosclerosis from hypertension. Early signs of both are vein displacement, vein indentation, sometimes a dilatation of the vein between the artery constrictions, an increasing visibility of the artery wall and a coppery reflex, which later becomes a silvery gray and still later a white streak; or, and clinically this is easily demonstrable, the entire artery tree straightens and contracts or the reverse happens and the arteries become more tortuous.

To complicate the picture of arteriosclerosis and hypertension further, exudates appear. Some are irregularly placed yellowish ones; others form a circle, and when the macula is included within its boundaries it is called retinitis circinata. A similar exudate crown may be remote from the macula, three distinct rings have been seen in the same eye and two are frequently found. If this does not afford sufficient confusion, the modern treatment of diabetes has so prolonged the life of thousands that they enter the arteriosclerotic time of life.

Before leaving the subject of changes in the retinal blood vessels, I wish to place special emphasis on three correlated and yet sometimes separate conditions. One is malignant hypertension characterized by progressive edema of the disk and an increasingly high blood pressure which does not respond to treatment, frequently

leads to early death and occurs in young males more often than in females. The second is the toxemia of pregnancy, with which the retinal expression follows a rather narrow, prescribed course, starting with an isolated spasm of one of the secondary or tertiary branches of the retinal artery. If the underlying cause is not removed, the spasms involve more branches and become more frequent, they become fixed, the hypertension increases and the usual and ordinary signs of retinal hypertension become manifest. It is therefore imperative that in all cases of toxemia of pregnancy the fundus be examined by a competent ophthalmoscopist who has the requisite knowledge to give advice regarding the management of the patient and to decide when the uterus should be emptied.

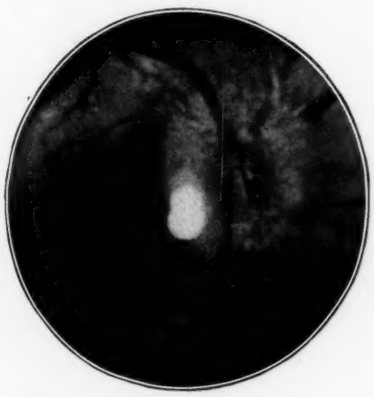


Fig. 14.—Brain tumor, left acoustic neuroma, right eye of a woman aged 37; swollen disk and surrounding retina, full veins with paralleling exudate. Papilledema.

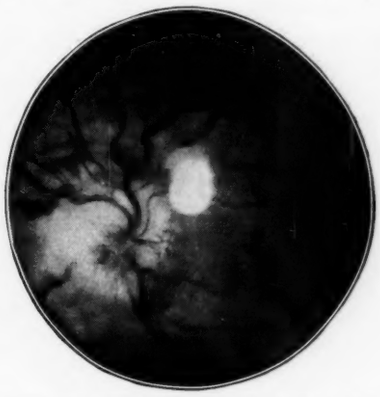


Fig. 15.—Papilledema (choked disk), left eye of a woman aged 60 with left acoustic neuroma; swollen, pale, elevated nerve head.

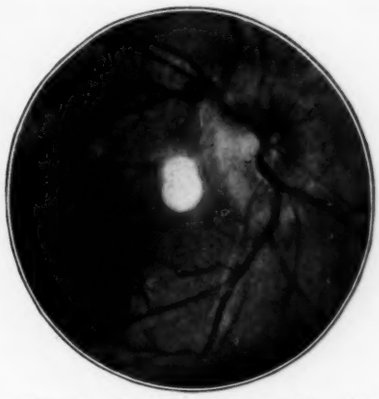


Fig. 16.—Syphilitic optic neuritis, right eye of a man aged 41; elevated gray disk, marked visual loss and field constriction, prompt response to mercury and iodide.

The third particular fundus picture is that which develops in the course of malignant endocarditis. It is characterized by flame-shaped hemorrhages, usually with white borders or white centers. These are of considerable diagnostic import, for the patient usually dies shortly after they appear.

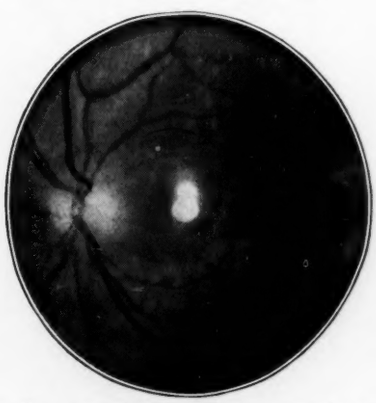


Fig. 17.—Retinochoroiditis disseminata, right eye of a woman aged 62; depigmented rounded areas of choroidal absorption.

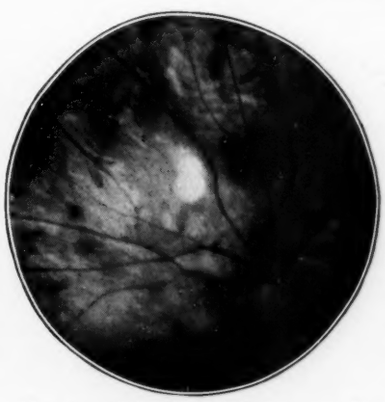


Fig. 18.—Retinochoroiditis, left eye of a man aged 50; apical abscesses, teeth removed, large choroidal scar.

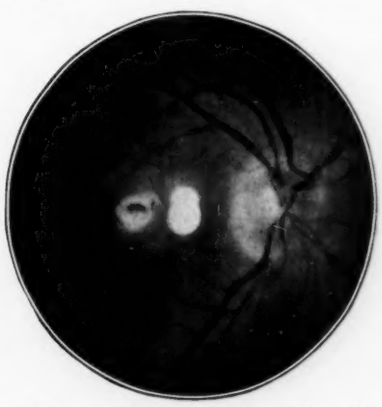


Fig. 19.—Tuberculous choroiditis, right eye of a man aged 35; two attacks of central choroiditis; the older lesion is the more heavily pigmented.

Diabetes may be severe, last for years and finally cause the death of the patient without producing retinitis. This is a very important point for all physicians to remember. On the other hand, the fundus picture of hard, yellow deposits near the disk or macula combined with small striate or globular hemorrhages may be the first visible evidence of something abnormal and lead to the investigations which disclose the correct diagnosis. There is considerable controversy regarding true pathognomonic, infallible diabetic retinitis, and, while inclined to believe that all the changes found in the fundus of a patient with diabetes can be duplicated in a nondiabetic person, I admit that the picture of yellow exudates arranged without order and not of uniform size, associated with hemorrhage without marked vessel changes, most strongly suggests diabetes. My photographic observations, however, do not warrant the conclusion that this pattern is always and not only caused by diabetes.

Furthermore, it is a matter of substantiated, reliable observations that high blood pressure and subsequent arteriosclerosis are concomitant with or even caused by the diabetes. Surely enough has been said to prove the necessity of complete physical and laboratory examinations whenever exudates and hemorrhages are found in the fundus.

Papilledema, or choked disk, is a prominent swelling confined to the disk and immediately contiguous parts of the retina. The central excavation is always demonstrable on stereoscopic examination. In cases of recent involvement the surface is vascular, while in cases of old involvement it is capped with a gray wool-like membrane. Papilledema should be considered a sign of intracranial pressure, caused by either an excess of fluid or a tumor, until proved otherwise. If a brain tumor is the first thing suspected, lives will be saved and vision preserved by the prompt recognition and treatment or exclusion of a neoplasm. Choked disk can usually be distinguished from optic neuritis if a careful history is taken, for in neuritis loss of vision is the first complaint and then field restriction and finally the ophthalmoscopic changes are uncovered, whereas choked disk is often discovered in the routine search

for the cause of general symptoms such as headache, and the field changes and visual loss are then revealed.

Syphilis has been sufficiently publicized to need little in the way of further remarks, but there are two special fundus manifestations worthy of comment: 1. Retinochoroiditis as it progresses through a period of an indefinitely outlined swelling to one of paling and flattening to end as a pigmented choroidal white scar.

Fig. 20.—Retinitis in pernicious anemia, right eye of a woman aged 47 who was seriously ill. The rounded, thick retinal hemorrhages are most suggestive of the blood state.

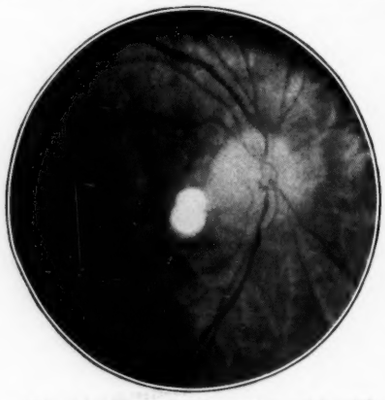


Fig. 21.—Retinitis pigmentosa with night blindness, right eye of a man aged 30; marked contraction of the visual field, retinal reflex greenish, disk of a waxen pallor, constricted arteries and veins. The pigmentation is just beyond the limits of photograph.

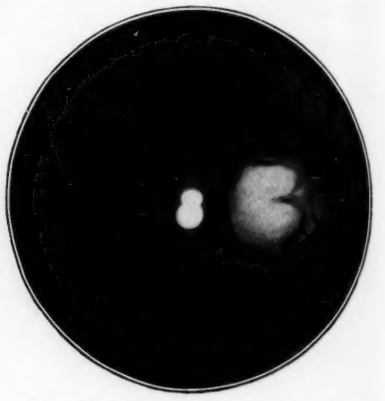


Fig. 22.—Glaucoma, right eye of a man aged 53 who was blind; a complete glaucomatous undermining cup of the nerve head.

This is evidence of a severe secondary stage. A patient who has had syphilitic retinochoroiditis seems immune to neurologic syphilis, for I have never seen such a patient have cerebrospinal symptoms. 2. Atrophy of the optic nerve, usually of the locomotor ataxic type, in which in a most unrelenting manner sight is destroyed by the steady decrease in the size of the visual field. There is a ray of hope for the patient if the modern treatment is administered, but the majority of the afflicted are doomed to darkness after the process is once inaugurated.

Somewhat similar to syphilitic choroiditis is that caused by tuberculosis, which strangely enough frequently attacks those who are considered to be in the full bloom of perfect health. The isolated lesion starts as a small pale area often adjacent to a blood vessel; other tubercles may form, coalesce, heal and recur, or a large conglobate tubercle may be present from the beginning of the fundus disease. Two facts confirmed by repeated observations assist in the diagnosis; one is the relatively slight pigmentation about the lesion and the other is a curious light reflection, a faint phosphorescence, from the thick vitreous opacities.

Many of the blood dyscrasias produce fundus hemorrhages with or without exudate.

Vitamins are widely advertised, and suggestive theoretical indications are often dogmatically expressed as therapeutic realities. A recent phase of this expanding work has led some physicians and many laymen to believe that night blindness is dependent on absence of vitamins and that the administration of the deficient elements will restore sight. This optimistic outlook has led to heartbreaking depressions in those suffering from genuine retinitis pigmentosa, choroideremia or the nyctalopia of myopia. These changes in the fundus are readily diagnosed and are not influenced by treatment with vitamins. The only partial loss of night vision that is benefited by the administration of vitamins is transitory and as yet without demonstrable alteration in the human fundus. Recently it has been reported that animals have shown appreciable pathologic changes.

Finally, the routine ophthalmoscopic inspection of every patient will lead to the earlier detection of glaucoma, which is one of the most serious of all eye diseases. Some day a campaign to prevent glaucoma by the early recognition of field defects and disk changes will be started. The time is opportune, and the need of public instruction far surpasses many of the overworked fads which take energy and money.

Every physician knows that in glaucoma the central depression in the disk increases in size until in the far advanced stage the entire nerve head is a sunken white cup and the patient incurably blind.

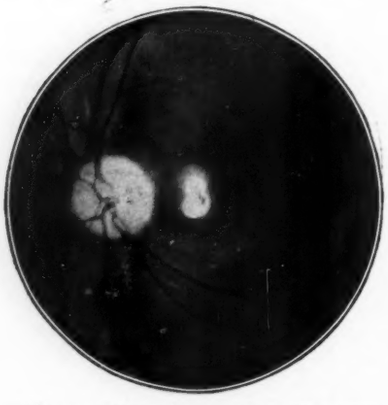


Fig. 23.—Traumatic atrophy of optic nerve, left eye of a man aged 24, sixteen years after automobile accident. The white nerve head is distinctly outlined. Arteries and veins maintain their normal size and relationship.

Fig. 24.—Senile macular degeneration, left eye of a woman aged 70; large, yellow, elevated circumscribed mass in the macula.

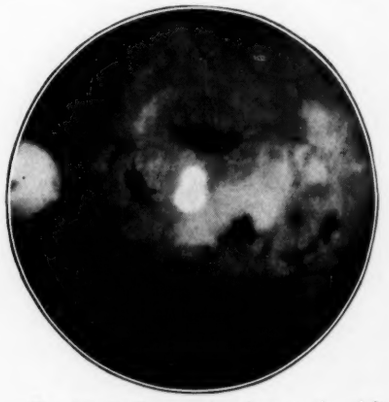


Fig. 25. Senile macular degeneration, left eye of a woman aged 70; large, whitish yellow irregularly pigmented macular scar.

Elderly patients frequently complain of inability to read; this is often correctly ascribed to faint lens opacities or partial atrophy of the optic nerve, but sometimes it is caused by a degeneration in the macular region. The earliest signs are recurring perimacular hemorrhages in one eye and then after months or years in the other. This eventuates in the destruction of the central retina and, although the patient is unable to do close work, he never goes blind. A most consoling fact. The seriousness of this situation calls for the mobilization of all physicians in an attempt to understand the method of production, the various stages and, if possible, combat the underlying factors, which at this time seem to be vascular and beyond the range of therapeutic agents.

This article was conceived as a review of actualities to stimulate every physician to use his ophthalmoscope, to recognize his limitations, to call for consultations and by cooperation to continue to uphold the high standard of American medicine, which is second to none because it combines individualistic enthusiasm with scientific accomplishments. When the individual is suppressed productive research always suffers, and this in turn adversely affects the health of the people.

Furthermore, it was intended to concentrate attention on the ocular fundus as one of the most available regions in the entire human body for the recognition of incipient, advancing and destructive processes.

To the initiated examination of the fundus discloses important clinical signs, which, when gathered together, form part of the life record of the patient. From the knowledge gained by the study of thousands of such reports, accurate prognostic as well as diagnostic conclusions can be drawn.

344 State Street.

Special Article

CONFERENCES ON THERAPY

TREATMENT OF SECONDARY SHOCK

NOTE.—*These are actual reports, slightly edited, of conferences by the members of the Departments of Pharmacology and of Medicine of Cornell University Medical College and the New York Hospital. The questions and discussions involve participation by members of the college staff, students and visitors.*

DR. MCKEEN CATTELL: In any consideration of the management of secondary shock, a knowledge of the signs and symptoms is an essential prerequisite. Theories of the causation of shock are numerous and diverse. Many of the characteristic changes associated with this condition have been satisfactorily explained. In general, these changes are progressive and serve as a guide to treatment and a measure of the severity of the condition.

The syndrome of secondary shock when fully developed is characterized by the following features: low blood pressure, decreased blood flow, decreased blood volume, lowered temperature and lowered metabolism. Hemoconcentration is an important feature and results in high hemoglobin values. The blood sugar and nonprotein nitrogen are increased, chlorides are decreased and the carbon dioxide combining power is low.

These changes are not all present in the beginning and for that reason the condition has commonly been divided into primary and secondary stages. The syndrome of secondary shock supervenes whenever a low blood pressure or inadequate circulation is allowed to persist. It is important to recognize that there are many causes of low blood pressure, and the end result is much the same whether the low pressure is due to hemorrhage, traumatic injury, burns, nervous manifestations, adrenal insufficiency, diabetic coma, cardiac failure, acute abdominal conditions or the action of toxins such as histamine and many others. All result in a lowering of the blood pressure, and in the initial stages of circulatory collapse there is a condition which is called primary shock. The changes characteristic of secondary shock are undoubtedly initiated at this time, but they develop gradually, usually over a period of several hours. The serious feature of any condition causing a fall in blood pressure is the reduction in the blood supply to the tissues; the patients consequently suffer from an inadequate supply of oxygen, and further damage is done to the circulation. A vicious circle is thus set up. Through various secondary readjustments the body tends to maintain blood pressure in the face of blood loss or other damage, so that when it falls below normal limits we may be certain that the safety factor is exceeded and that there is danger of a serious deficiency in the circulation. It has been shown experimentally that when the blood pressure has fallen to about 80 mm. of mercury it is not adequate to maintain the normal functions of the tissues. Active therapeutic measures should be instituted before such levels are reached.

The evaluation of therapeutic measures requires a consideration of the mechanism by which the changes characteristic of secondary shock are brought about, and we need especially to know which of the various factors responsible for maintaining the blood pressure are at fault.

There is no evidence whatever that in this condition the heart is in any way inadequate to meet the demands made on it. If it is given fluid it will effectively pump that fluid against even a very high pressure, and thus there is no reason to administer cardiac stimulants.

The vasomotor center continues to act in a normal manner; in fact, it has been shown experimentally that the center is usually in a state of heightened activity, thus tending to compensate for the lost blood and maintain a normal blood pressure. It is true that in advanced shock the vasomotor center along with the other centers does fail, but this occurs only after the pressure has been low for a long period and represents a terminal condition.

An outstanding feature is a diminution of circulating fluid. The blood vessels contain less than the normal quantity of blood, and the amount returning to the heart is much reduced. Where is the lost blood? In the case of hemorrhage the answer is obvious, but an essentially similar condition occurs in shock without hemorrhage. There is general agreement among physiologists that a reduced circulation results in damage to the capillaries. They are dilated and they apparently become more permeable; at any rate, filtration is abnormally rapid and the blood vessels are unable to retain fluid. The changes are similar to those occurring locally in the formation of a wheal.

Gradually the blood volume is reduced, and the signs and symptoms of secondary shock become increasingly

prominent. The pressure falls and the various compensation mechanisms are brought into action. The fall in blood pressure stimulates the afferent endings in the carotid sinus and elsewhere and the heart rate is thus reflexly increased and the arterioles are constricted. The fluid loss brings about an increased concentration of cellular elements; kidney function is reduced because of the decreased blood flow and low pressure with a resulting increase in blood urea. In addition to increased cardiac rate and vasomotor tone there is other evidence of increased sympathetic activity in the increased blood sugar and sweat secretion. The latter promotes heat loss and, along with the lowered metabolism, explains the drop in temperature. There is general agreement that acidosis is a consequence of decreased oxidation due to circulation deficiency.

Moon, in his recent book on shock, has defined the condition as a circulation deficiency, not cardiac or vasomotor in origin, characterized by a decreased volume of blood, reduced cardiac output (volume flow of blood) and hemoconcentration. The points of attack on this problem from a therapeutic standpoint would appear to be two: The first is to increase the circulating volume of fluid, and the second is to prevent the fluid loss from the peripheral vessels. There is very little basis for the employment of the so-called circulation stimulants. General measures directed toward the conservation of heat and fluids, and also for the promotion of rest, are of the utmost importance and should be given first place in any regimen for treatment and prevention of secondary shock.

THE MANAGEMENT OF SHOCK

DR. JOHN E. DEITRICK: The clinical picture of the fully developed case of secondary shock is unmistakable. It is essentially the same irrespective of the underlying cause of the shock. As has been indicated, the disintegration of circulatory function which goes under the name of shock does not have only one cause but many causes. We do not know what these primary disorders possess in common which leads to the same ultimate outcome, namely shock, if indeed there is any such common factor. The significant fact is this: regardless of the clinical condition in the course of which secondary shock occurs, the clinical signs and symptoms, as well as the physiologic derangements of the circulation, appear to be essentially identical in all of them when the state of shock is present.

I may speak briefly, therefore, concerning the outstanding clinical characteristics of shock, especially concerning those which have a direct bearing on the objectives of our treatment. These are: 1. Diminished blood volume. There is of course a diminished blood flow but it is primarily due to the diminished blood volume. 2. Decrease in sodium chloride of the blood. 3. Diminished carbon dioxide carrying capacity of the blood (diminished alkali reserve). 4. Paralysis of the capillaries and extreme degrees of constriction of the arterioles. Dehydration with loss of salts and blood proteins are outstanding phenomena in shock. The abnormal permeability of the capillaries appears to be such that the injection of fluid disappears from the circulating blood with extreme rapidity, even though the blood is concentrated and is greatly in need of the injected fluid.

The appearance of the patient is that of one who is desperately ill. There is extreme prostration. There is apathy or restlessness and anxiety. The facial expression is often pinched. The skin is very pale and often shows a grayish cyanosis. It feels cold, clammy and moist. There is sweating. The peripheral veins are collapsed. Rather marked thirst is often present. The pulse is rapid and thready. The temperature is subnormal and the blood pressure is extremely low, sometimes almost impossible to record. As the condition progresses the respiration begins to suffer; it becomes shallow and feeble. Respiratory failure seems to be commonly the immediate cause of death. I have seen the heart continue to beat for five or ten minutes thereafter, and even longer when artificial respiration was administered.

The treatment of secondary shock, for the most part, is independent of its immediate cause. Since the blood is stagnating in the periphery and is cooling off rapidly, measures are taken immediately to maintain the body temperature. We wrap the patients in warm blankets and we apply hot water bottles and the electric pad for that purpose. In order to promote better circulation in the brain we raise the foot of the bed above the level of the patient's head.

A large blood transfusion is the most satisfactory way of restoring the blood volume. The restoration of the blood volume is the most important single measure. Most patients will fail to recover in shock if their blood volume has been reduced by as much as one half of their normal. Substitutes for blood transfusion are not as satisfactory. A useful emergency agent which can often be obtained sooner than the blood transfusion is dextrose. An injection of 50 cc. of a 50 per cent solution sometimes produces a beneficial though fleeting effect on the circulation. It may be followed by larger amounts of saline and 5 per cent dextrose solution given as a continuous intravenous drip at the rate of from 1 to 10 cc. per minute. These infusions all lack the protein which helps to keep them in the circulating blood. There is danger in their use in that the large quantities of rapidly diffusible fluid with low osmotic pressure promote pulmonary edema.

A 6 per cent solution of acacia was used during the war to combat the shock of war wounds. This solution produces more lasting increase in the blood volume. I do not favor it particularly, however. I hope the pharmacologists will discuss this substance.

The respiration in patients with shock is very shallow. The carbon dioxide combining power of the blood is low, namely 20 or 30. Because of the acidosis the Boston group has recommended and reported beneficial results from the use of a 5 per cent solution of sodium bicarbonate intravenously. They have also recommended the inhalation of carbon dioxide for periods of five minutes at intervals of five minutes. Both of these measures tend to increase the depth of respiration and promote the return of blood to the right side of the heart.

Morphine sulfate is indicated only when the patient is restless or in pain. The danger of depressing the respiratory center by morphine during shock is considerable. I have seen one patient die of morphine during shock. It should not be used for the patient who lies quiet.

Drugs are generally of questionable value in shock. Digitalis is distinctly contraindicated. Epinephrine is of no value and may be dangerous because it constricts

the arterioles which are already constricted in shock. Caffeine is widely used as a stimulant in shock and it apparently exerts some beneficial effect. Strychnine has been employed but the pharmacology of strychnine leaves little to justify its application in the treatment of shock.

It cannot be emphasized too strongly that early treatment holds out the only hope of success in patients with shock. When a patient begins to show peripheral circulatory disturbances which are known to terminate in shock, that is the time to begin treatment. Treatment should be started when the falling blood pressure has fallen only to 90 rather than to 60 or 70. It is preferable to begin treatment in the stage of the primary shock, namely the stage in which the blood pressure has fallen, but before paralysis of the capillary bed has taken place. In the case of severe hemorrhage showing some of the symptoms of shock an intravenous infusion of physiologic solution of sodium chloride may cause marked improvement, but if the low blood pressure has been allowed to continue for a long time with the consequent secondary increase in the permeability of the capillaries the infusion of saline solution may be of no value at all. As has been stated, there is a stage in shock when the capillary permeability is so great that proteins pass readily out of the blood stream; the resulting change of the osmotic pressure of the blood makes it impossible for the blood to hold the injected fluid. In a sense it may be said that measures applied to the prevention of secondary shock in case of failing circulation provide the best outlook. When the patient is seen in a later stage, however, that is, in a stage in which secondary shock is already present, the sooner the treatment the better the results, for the longer the state of shock is permitted to exist the more difficult it becomes to correct it and the higher is the mortality.

PHARMACOLOGY

DR. CATTELL: Dr. Deitrick has mentioned a number of drugs which have been commonly employed in the treatment of shock, but he has left the impression, quite correctly I think, that they represent a comparatively unimportant part of the management of the condition. I had hoped he would commit himself in favor of the use of some of those substances so that I should have had the opportunity of pointing out the lack of a sound experimental basis for their employment.

Of the many drugs which have been used in shock I have time to consider only one or two. A substance of special interest in the treatment of this condition is acacia, because that is a substance which has been very extensively employed in the replacement of lost blood, particularly during the war, when it was often impossible to undertake the more elaborate procedure of blood transfusion.

From a theoretical standpoint acacia appears to be an almost ideal substitute for lost blood because it has a large colloidal molecule which is retained in the blood stream and gives the desired increase in osmotic pressure. Its use was considered at one of our recent conferences in connection with the matter of raising the osmotic pressure of the blood for the removal of edema in nephrosis. It has been successfully employed in many other conditions, particularly in shock and hemorrhage, but severe reactions have been frequent and the question arises as to its suitability for routine use. Particularly during the war, numerous severe reactions were experienced and there is no doubt that many injured men were killed by the use of acacia. I have seen many that appeared to come under that classification. On the other hand, dramatic results were often achieved in raising of the blood pressure and no bad effects followed. The question of untoward reactions has received much attention, and at the time of the war it was noted that there was a good deal of variation in the effects of different lots of acacia. It was assumed that impurities played an important part in the reactions, and I believe that nowadays when much more highly purified preparations are available bad results are not nearly as common.

But animal experimentation has emphasized the existence of certain drawbacks in the use of acacia, and I would like to mention one or two recent publications on this subject. In the first place, the matter of elimination is important. It has long been known that the elimination of acacia is slow, and this is one of the reasons for its therapeutic value. Acacia is retained in the blood stream for several days and is only gradually eliminated from the body. But small amounts of the total injected can be recovered from the urine and it is not oxidized.

The elimination of acacia was recently studied by Andersch and Gibson of the University of Iowa. In a series of eight rabbits they examined various organs to find out where this material was stored and were able to recover from the liver on the average about 50 per cent of the total amount of acacia injected. Analyses made several months after the injection of the acacia showed a large percentage of the total amount injected to be still present. They also made histologic studies and got evidence indicating that this was not entirely an innocuous condition. The cells were full of vacuoles, presumably containing the acacia, and there was definite interference with the formation of bile. The same thing was true in rats and dogs and in one human being whom they examined. This patient had received acacia over a period of several months, and more than 40 per cent of the total acacia injected during that period was recovered from the liver. Further, in regard to the manner of excretion it is of interest that acacia was found to be eliminated in the bile and thus gradually excreted.

There is the further fact that in using acacia rather than whole blood one is not using the most favorable possible substance, because the oxygen-carrying capacity of the blood is not thereby increased. This point has been emphasized by Yandell Henderson, who carried out experiments on dogs bled a certain standard amount, causing approximately 50 per cent of them to die if not treated. In those animals, all of which recovered if blood was reintroduced, the chances of survival were not improved by the use of acacia. For that reason Henderson emphasized the importance of the red blood corpuscles in the treatment of shock and he thought that they constitute an essential part of any procedure for replacing lost blood.

Perhaps it will be just as well to leave the remainder of the period for discussion, and if there are points that come up in connection with the other substances mentioned by Dr. Deitrick I think several of us are prepared to say something about them.

DR. HENRY B. RICHARDSON: If a dog receives acacia and nothing else, what is the effect on its longevity?

DR. CATTELL: That was not studied in the experiments referred to. However, I think no bad results have been reported from the injection of acacia into animals other than the type of finding reported by Andersch and Gibson. Those animals were not killed by the acacia.

STUDENT: I wondered if there was any experimental evidence supporting the use of caffeine as a cardiac stimulant.

DR. CATTELL: I think that the use of caffeine rests on a very unsound experimental basis. I am not familiar with the clinical experience in the use of caffeine, but from a pharmacologic standpoint it can be said with a good deal of emphasis that it has no value as a circulatory stimulant. The actions are rather mixed, there being a central action which tends to cause constriction of the peripheral vessels and a slowing of the heart, and a direct action on the musculature of the arterioles causing them to relax. The net effect on blood pressure is very slight. I believe that in therapeutic doses no appreciable action could be expected from the use of caffeine. Its use as a respiratory stimulant might be considered. I feel that in shock there is very little indication for the use of respiratory stimulants because in general there is no evidence that the circulating blood contains less than the normal saturation of oxygen on leaving the lungs, and the slow respiration is probably to a considerable extent secondary to the general depression of bodily functions.

STUDENT: Is the profound psychic depression due to anoxemia and low pressure or is there any experimental evidence showing that there is edema in the central nervous system causing a depression in shock?

DR. CATTELL: I think there is an adequate basis for the depression in the generally reduced level at which activities are carried on under the circumstances of a deficient circulation.

STUDENT: I should like to ask Dr. Cattell, in line with what he said about caffeine, whether the diuretic action of caffeine, by increasing the dehydration, is contraindicated.

DR. CATTELL: I think not. In a condition of this sort where there is dehydration a diuretic is usually ineffective, and, while I cannot speak from experience, I should feel that that would not be an important consideration.

DR. DEITRICK: I have seen caffeine and epinephrine given by intracardiac injection when the patient's respiratory center had ceased functioning for ten minutes and the patient's respiratory rhythm was reestablished for another half hour. Dr. Wolff saw the patient with me along with several others. There was no doubt that the respirations had absolutely ceased. We were giving artificial respiration while the nurse was getting the caffeine and epinephrine ready. The respiratory rhythm came back after injection but the result was only temporary and we could not maintain it.

DR. HARRY GOLD: The stimulant action of the xanthines on the respiratory and the higher centers is really very striking sometimes. In patients with uremic coma and patients with Cheyne-Stokes respiration as a result of advanced heart failure, consciousness is restored and Cheyne-Stokes respiration is abolished. Consciousness is sometimes restored for a period long enough to enable the patient to sign his will.

DR. BRUCE HUNT, Perth, Australia: What preparation is used?

DR. GOLD: Caffeine with sodium benzoate in a dose of about 1 Gm. intravenously, but injected slowly, taking two or three minutes for the injection, or aminophylline in a dose of about 0.25 or 0.5 Gm. injected intravenously. A contraindication to the use of caffeine one might possibly find in the observation of Grollman, namely that the cardiac output is increased by large doses of caffeine but the oxygen requirements are increased to about the same degree; about 20 per cent increase in oxygen uptake, associated with an increase in cardiac output. The drug is therefore imposing an added load on the heart rather than relieving it.

STUDENT: I should like to ask Dr. Deitrick whether there is a toxic substance liberated in an injured limb and how effective a tourniquet might be.

DR. DEITRICK: Work has been done on that. If you crush a limb tying the artery first, the animal will not go into shock. If you tie the vein leaving the artery intact and crush the limb, the animal will go into shock. That is important. The best observers have been unable, however, to demonstrate a substance which is carried in the blood and which will produce shock or even a drop in blood pressure, such as histamine-like substances in the blood of the femoral vein of a crushed leg. Histamine shock at autopsy gives quite a different appearance from that of a patient dying from shock following blood loss.

DR. EUGENE F. DU BOIS: Dr. Cattell, have you any comments to make on that? I want to introduce a little divergence of opinion in this discussion.

DR. CATTELL: I feel that that possibility would be very difficult to rule out. It is of interest that recently there have been reported by Feldberg experimental studies in which an increase in histamine has been demonstrated in shock produced by snake venom and by certain bacterial toxins. The amounts of histamine are extremely small. However, large amounts may not be required to produce damaging effects when liberated over a period of several hours. I believe that our methods of determining histamine are so crude at the present time that it would be extremely unlikely that such a demonstration could be made. It is important, nevertheless, that in cross transfusion experiments this type of reaction cannot be easily demonstrated, an observation which would seem to imply at least that under favorable circumstances the animal will be able to cope with whatever quantities of histamine may be formed.

DR. DU BOIS: Do you think histamine is an important factor in medical and surgical shock?

DR. CATTELL: In experimental shock Dr. Cannon and I thought that histamine might play a part, but I think the proof for that is yet to be obtained.

DR. DEITRICK: Histamine can be detected if injected into an animal in small amounts, that is in an animal that has a crushed leg. If the venous blood returning from that leg is injected into another animal a fall in blood pressure occurs, but no similar effect has been demonstrated in blood from the crushed leg itself. I

think that Dale agrees there is very little evidence that histamine has any real effect in traumatic shock.

DR. CATTELL: It is interesting that the liberation of potassium has been recently considered as a cause of shock. At Columbia, Scudder and his associates feel that potassium set free in tissue damage is important. As you know, potassium is present in relatively high concentrations inside the cell, a matter of 300 or 400 mg. per hundred grams of tissue as compared with only about 20 mg. per hundred in the blood, and therefore the release of a relatively small proportion of that present would bring about a toxic concentration in the blood stream.

DR. RICHARDSON: Is there a change in the concentration of sodium chloride analogous to that in Addison's disease?

DR. GOLD: There is a fall in the sodium content of the blood serum in shock. Isn't salt useful in the treatment of shock?

DR. DEITRICK: We prefer to use sodium bicarbonate in order to supply the sodium ion. The carbonate may be lost through the lungs as carbon dioxide. Its use would tend to increase the alkali reserve.

DR. DU BOIS: Dr. Deitrick, I should like to ask a few questions about the amount and strength of dextrose or saline solution that you give, whether or not you give them in combination, and also the method of preparing relatively sterile solutions of sodium bicarbonate.

DR. DEITRICK: I will answer the last question first. I have had to prepare sodium bicarbonate solutions on several occasions. I don't know how the Boston group prepared their solution. We use sterile doubly distilled water and simply add the sodium bicarbonate to it to make a 5 per cent solution. You cannot add the sodium bicarbonate and then sterilize it for if you do the salt is broken down.

As to the dextrose or saline solution, you can use either. I would use 5 per cent dextrose or physiologic solution of sodium chloride or sometimes even a mixture of the two. Their action is very transitory, so I think they ought to be used only until you can get blood or acacia. I would not have any objection to using acacia to tide the patient over, but I would not want to keep on giving acacia. It comes in large sealed ampules, and I have given it to patients in cases in which I think there is urgency in the face of a falling blood pressure. Blood banks may make it simpler to treat these patients in the future.

DR. DU BOIS: I presume you all know what a blood bank is. It is an accumulation of many varieties of blood in an icebox so that almost any need can be supplied.

Before leaving this subject, I presume that in preparing the bicarbonate you put into it the cooled water, so that there would be no danger of its changing into a carbonate, and that you ladle it out from a clean container.

DR. HUNT: Do you find any practical justification for the use of the hypertonic saline in preference to the regular saline solution?

DR. DU BOIS: I was going to ask that question and also about hypertonic dextrose. Can you withdraw some of the fluid from the tissues by using the stronger concentration of dextrose?

DR. DEITRICK: Yes, there is experimental work indicating that you can. As concerns hypertonic saline solution I think it can be shown that it will increase blood volume for a period of perhaps fifteen or twenty minutes, and then the effect is lost. Some change seems to occur, however, so that the loss of fluid from the blood from then on becomes more rapid. I don't understand why but this has been shown by careful work.

DR. DU BOIS: There is also the possibility that in using the too concentrated solution of dextrose you might produce a glycosuria and diuresis.

DR. GOLD: What about the thrombophlebitis caused by concentrated solutions of dextrose, the 50 per cent solutions?

DR. DEITRICK: I have seen thrombosis produced after only one injection of a concentrated solution of dextrose, and if you repeat the injections in the same vein it almost always occurs.

STUDENT: What concentration of saline solution and of dextrose would be given?

DR. DEITRICK: We usually use 5 or 10 per cent dextrose. Large amounts of this fluid are not without danger. In experiments on dogs large injections of dextrose and saline solution have caused death with pulmonary edema. Physiologic solution of sodium chloride (from 0.85 to 0.9 per cent) is the one we commonly use.

DR. HUNT: What is the routine on this procedure in the emergency ward?

DR. DEITRICK: We have saline and dextrose solutions which we can get within five minutes. I don't believe there is any acacia available in the accident room now, is there?

INTERN: Not that I know of.

DR. GOLD: I should like to ask Dr. Deitrick when he considers or by what signs he considers the patient in whom the blood pressure has fallen to be in a state of secondary shock. Where does one draw the line?

DR. DEITRICK: I think that in the interest of good therapy we ought to define shock as existing before the typical picture develops. Shock, to me, already exists when the blood pressure has dropped to 70 and when the blood volume reaches 50 or 60 per cent of normal. The hemoglobin determination proves misleading because it may be high as the result of concentration of the blood. I don't believe a patient should be allowed to remain with a systolic pressure of 90 without something being done to increase it. How one proceeds depends on the rate of the fall of the blood pressure. If you are watching a patient who is bleeding and the blood pressure is 100/60 and an hour later it is 100/50 and in twenty minutes later it is 90/50, I think it is now time to intervene. It is not so serious if blood pressure falls more slowly to 90 over a period of six or eight hours and then begins to level off. One ought to keep a very accurate graph of what is happening to the blood pressure and pulse, so that one may see how rapidly the circulation is changing. If it is changing rapidly, I wish to step in much sooner than if it is changing slowly. In a case of internal hemorrhage, the body should be given a chance to compensate for a hemorrhage and to stop it. When to interfere is a matter which requires considerable judgment and as full a knowledge as possible of the course of events in the individual case.

Council on Physical Therapy

THE COUNCIL ON PHYSICAL THERAPY HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORTS. HOWARD A. CARTER, Secretary.

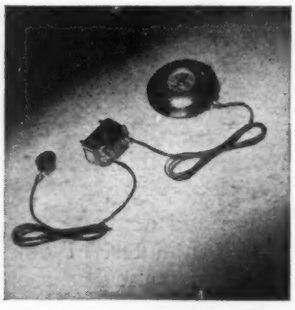
WESTERN ELECTRIC AUDIPHONE ORTHO-TECHNIC MODEL ACCEPTABLE

Manufacturer: Western Electric Company, 195 Broadway, New York.

The Western Electric Audiphone, Ortho-Technic Model, is a carbon microphone hearing aid. It is assembled from parts designed to provide different frequency response characteristics. After the individual's hearing loss has been measured the parts are selected which will best meet his requirements. The equipment consists of microphone, air and bone conduction receivers, amplifier, batteries (supplying 3 and 4½ volts), head band, cords and receiver tips. The parts are finished in polished black.

The unit was tested by a competent investigator and the following report made:

Microphones.—Two carbon particle barrier type microphones, lentil shaped with disk diameter of 3 inches and thickness of three-fourths inch, were submitted. The carbon chamber in these units is filled full of carbon particles instead of three-fourths full as in the ordinary and earlier types. A four-spoked current control rheostat adjustment is on the front. An attachment slip is on the back, while a jack for a connecting cord is placed at the bottom.



Western Electric Ortho-Technic Model Audiphone

To test the frequency response characteristics of a microphone, it was included in a series circuit with a 4.5 volt dry battery and a 30 ohm resistor, since it had been previously established that the hearing aid circuit in which the microphone is normally used had a resistance of 30 ohms. Then the transmitter was placed in a sound chamber which was free from reflections and subjected to pure tones of constant intensity and varying frequency. The voltage across the resistor is a measure of the electrical output of the microphone, and this voltage was impressed on the input terminals of a cathode ray oscilloscope and measured as the frequency was varied. The results for the two microphones in question are shown on graph 1.

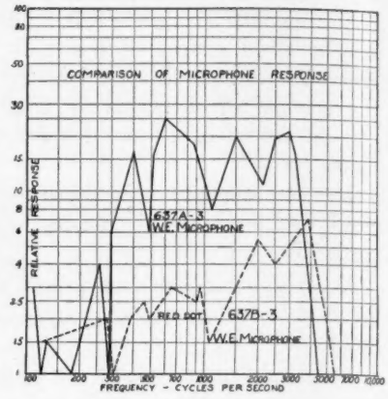
It will be observed on studying these curves that the principal difference between the two response characteristics is that 637A-3 has a larger output than 637B-3. The general trends of the two curves, however, are quite similar, certain characteristic peaks and valleys being present in both. It may be said, that, on the whole, the response is relatively well sustained over a frequency band of from 250 to 4,500 cycles per second, without the presence of extreme response peaks.

It was also possible to observe the wave form of the electrical output of the microphones on the oscilloscope screen and it was observed that the output was for the most part fairly free from harmonic distortion.

Air Conduction Receivers.—Three air conduction receivers were supplied. All are of the permanent magnet miniature type, furnished with a hard rubber tip which snaps onto the receiver and is intended to conform to the inner contours of the outer ear. The receivers are about seven-eighths inch in diameter and one-half inch deep with connecting cord jack at the bottom. The jack accommodates one large and one small pin so arranged that the polarizing current cannot flow in the wrong direction.

The receivers were tested individually as to frequency response by supplying them with current of varying frequency and at constant terminal voltage. The acoustic output of the receivers was impressed on an artificial ear. The electrical output of the artificial ear was then observed on a cathode ray oscilloscope. The results are shown on graph 2.

It will be observed by referring to the curves that receiver WE 709A-3 (marked with two dots) peaks at about 1,200 cycles and that receivers WE 709B-3 (marked with one dot) and WE 709C-3 (no marks) have response characteristics similar to A but with main resonant peaks shifted up in frequency by 400 and 1,400 cycles respectively. In the main it would be true to say that the B and C curves are similar to the A curve but are referred to different frequency scales.

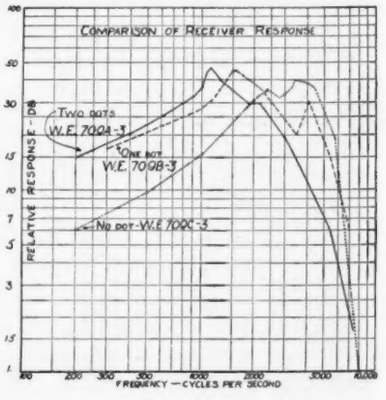


Graph 1.

Carbon Particle Amplifier.—The amplifier was made of molded bakelite approximately 1¾ by 1¼ by 1 inch in size. Through the bottom projected four split pins fitting into corresponding jacks in the battery. Receiver and microphone cords plug into poled jacks situated on the top of the amplifier, and at one end is an on-off switch. The amplifier was found to operate equally well in all positions and accordingly it is assumed to be a carbon particle barrier microphone magnetically operated. The battery used with the amplifier consisted of two separate 4.5 volt batteries held in one container and terminating in two separate jacks. The microphone circuit and the receiver circuit are entirely separate electrically, being coupled only in a mechanical sense in the magnetically operated microphone. The double battery arrangement eliminates the defect of singing due to electrical coupling entirely.

Battery Consumption.—When the amplifier and the two 4.5 volt batteries of the GB-4.5 battery unit were used, the current in the amplifier-receiver circuit was approximately 20 mils and in the microphone-amplifier circuit the current varied from 20 to 23 mils with rheostat full on. For the lowest rheostat setting the latter current was found to be 6 mils.

The measurements were repeated, the 3 volt GB-3 battery unit being used. A current of 9 mils was measured in the receiver circuit, and 14 mils and 4 mils in the microphone circuit for maximum and minimum rheostat settings respectively.


COMPARISON OF RECEIVER RESPONSE
RELATIVE RESPONSE - DB
TWO DOTS W.E. 709A-3
ONE DOT W.E. 709B-3
NO DOT-W.E. 709C-3
FREQUENCY - CYCLES PER SECOND

Graph 2.

Intelligibility and Articulation Tests.—The measure of actual usefulness of a hearing aid depends largely on the faithfulness with which sounds are amplified. Consequently a controlling element in any judgment of its merit must be its actual performance. Tests were accordingly conducted. One departure from the usual test method was made in that the output of the hearing aid, instead of being reduced in volume by an artificial ear circuit, was reduced in its own electrical circuit by a resistance pad so designed that the microphone operated with its rated current. The hearing aid receiver under these circumstances was not subjected to full speech current amplitudes, but it had been previously determined that the distortion introduced by the receiver was inconsiderable. The amount of speech volume loss introduced by the resistance pad in order to produce sounds in the ear of the same loudness as when directly listened to was taken as the measure of the hearing aid amplification. It is believed that this method of test is superior for the purpose to the one employing additional

transmission links with the necessary acoustic coupling devices. Experience indicates that the results obtained are consistent.

Both discrete sentence intelligibility and articulation tests were conducted, as well as an amplification determination. Owing to the number of receivers and microphones available, a rather large number of combinations is possible. From the response characteristics of the individual items a combination was selected which represented the one most favorable for normal hearing. It was later found, however, that the most extreme combination possible did not materially affect the conclusion. The results obtained is given in the table.

As an additional test a list of difficult, unfamiliar, telephone directory names with two initials was transmitted over the hearing aid. The results are given in the 5th column of the table. Also, in order to determine how much loss in articulation was produced by the room itself and the manaural listening method, a test was conducted as follows: The

Summary of Results

Hearing Aid Combination	Sentence Intelligibility	Con-Vow-Con Articulation			Difficult Telephone Directory Names with Two Initials	Intensity Gain in Decibels; Rheostat Setting, Maximum
		Con	Vow	Syllable		
No amplifier, microphone 637A-3, battery 4.5 volts.....	99.0%	87%	90%	70%	80%	5-10
Amplifier, microphone 637A-3, receiver 709B-3, battery 4.5 volts.....	99.5%	76%	90%	60%	70%	20-24
Test room only; direct conversation, one ear covered.....	.....	92.5%	95%	85%		

observer tightly covered one ear with a jar stuffed with yarn and listened to con-vow-con syllables spoken in a normal tone on the side of his covered ear. The results of this test are given in the last line of the table. It will be observed that there is a considerable loss, 15 per cent, in syllable articulation.

Bone Conduction Transmission.—Similar tests were conducted with the same items as shown in the second line of the table except that the receiver was replaced by the 710A-3 bone oscillator. The results obtained as to sentence intelligibility and articulation were almost identical with those in line 2.

In view of the foregoing report, the Council on Physical Therapy voted to include the Western Electric Audiphone, Ortho-Technic Model, in its list of accepted devices.

BURDICK SURGICAL DIATHERMY, MODEL D-3, ACCEPTABLE

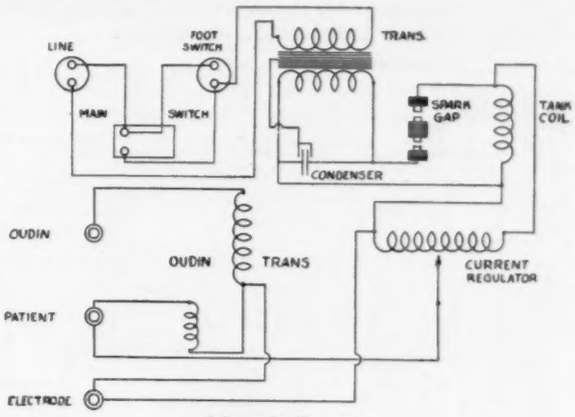
Manufacturer: The Burdick Corporation, Milton, Wis.

The Burdick Surgical Diathermy Unit, Model D-3, is recommended for surgical and for limited medical purposes. It is primarily a surgical unit producing currents for electrocoagulation and desiccation. It is adaptable for moderate diathermy use. This portable unit comes in a leatherette-covered cabinet with carrying handle on top. The dimensions are 14½ inches long by 10 inches wide by 6¾ inches high or 9½ inches high with cover. It weighs 25 pounds. There is a compartment in the cover for foot-switch, cords and electrodes. The standard equipment includes foot-switch and cords. Surgical electrodes are optional.

Burdick Surgical Diathermy, Model D-3.

Designed to provide a low voltage and high amperage current for electrocoagulation purposes and to produce an Oudin high voltage current for desiccation and fulguration, the unit operates by spark gap. Four three-eighths inch tungsten points mounted on radiators turned from solid stock have gaps in fixed position. The transformer is the low voltage, air-cooled type. Data submitted by the firm on temperatures observed for spark gap, transformer and cabinet interior, taken after six hour runs at full load, were within the limits of safety. The condenser is made of mica and copper plates. According to the firm, minimum high frequency losses occur with this resonator wound on bakelite tubing.

The intensity is regulated by means of a single control, the micro-inductive switch. This provides minute regulation of current from zero to the full range of the apparatus. The firm states that this precision control enables the operator to duplicate dosage by recording the settings used for a given size of electrode and certain type of work.



Schematic diagram.

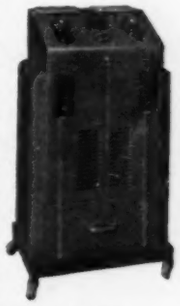
The unit was investigated clinically by a qualified physician and reported to give satisfactory service. However, it was pointed out that because of the length of the electrode handle, 14 inches, it is often necessary in performing fine work to slide the hand down over this insulated section to gain control of workmanship. The soft rubber insulation of the electrode tips does not prevent heating when a strong current is used.

In view of the foregoing report, the Council on Physical Therapy voted to accept the Burdick Surgical Diathermy, Model D-3, for inclusion in its list of accepted devices.

WAPPLER SHORT WAVE DIATHERMY MACHINE, MODEL C-507, ACCEPTABLE

Manufacturer: American Cystoscope Makers, Inc., Comprex Division, 450 Whitlock Avenue, New York.

The Wappler Short Wave Diathermy Machine, Model C-507, is recommended for medical and surgical diathermy, including hyperpyrexia treatments. It is similar to the Comprex Short Wave Diathermy previously accepted by the Council (THE JOURNAL, April 25, 1936, p. 1468) except for the addition of the inductance coil technic. The former model was investigated with pad and cuff electrodes. Due to the merging of the Comprex Oscillator Corporation with the American Cystoscope Makers, Inc., the name of the Comprex Short Wave Diathermy has been changed to Wappler Short Wave unit to conform with the established trade name "Wappler" covering all of the products of the American Cystoscope Makers, Inc. Storage space is provided by means of a drawer. The complete unit weighs 125 pounds.



Wappler Short Wave Diathermy Machine, Model C-507.

According to the firm, the circuit employed is identical in all respects with the two tube type used in the Comprex Short Wave Diathermy and has, in addition, an impedance matching circuit permitting inductance cable appliances. Both units have a 15 meter wavelength. The

Average Temperatures with Inductance Coil Technic

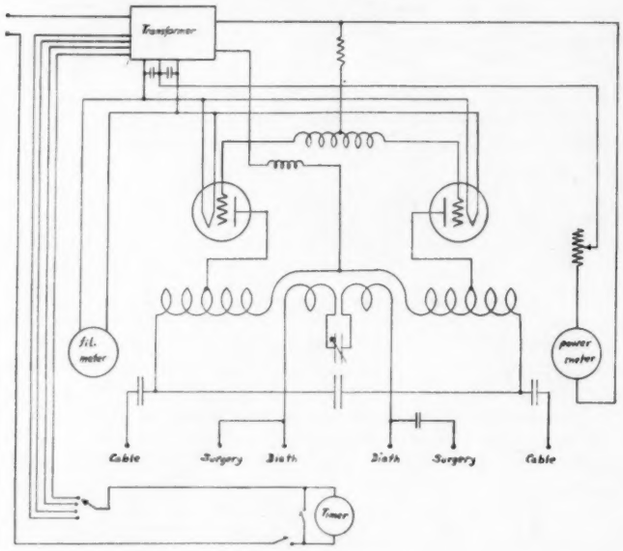
Deep Muscle		Oral	
Initial	Final	Initial	Final
98.1	105.3	99.6	99.0

transformer temperature rise and the rise at various levels within the cabinet, after a two hour run at full load, were low enough to satisfy the requirements for fire hazard. When the unit is

used with pad and cuff electrodes, it is claimed to perform exactly as the accepted model on the basis of the tests made on the circuit similar to that employed in the Comprex machine.

As evidence of the ability of the unit to produce deep heating, the firm submitted six tests performed with the thermocouple technic recommended by the Council.

Average temperatures for six observations with the inductance coil technic are given in the accompanying table.



Schematic diagram.

The unit was tried out in a clinic acceptable to the Council and performed satisfactorily.

In view of the foregoing report, the Council voted to accept the Wappler Short Wave Diathermy Machine for inclusion in its list of accepted devices.

Council on Pharmacy and Chemistry

REPORT OF THE COUNCIL

THE COUNCIL HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORT.

PAUL NICHOLAS LEECH, Secretary.

THE PRESENT STATUS OF CYCLOPROPANE

The Council stated in a preliminary report on cyclopropane [1] that the anesthetic could not be properly evaluated because adequate evidence was not available. Since then much clinical and pharmacologic evidence has become available. The evidence is considered in this report.

Seevers and Waters,[2] in their review of the pharmacology of anesthetic gases, note that when an attempt is made to list the qualities which are expected in the "ideal" anesthetic gas "the desires of four individuals must be considered." The patient desires a rapid induction without irritation or unpleasant odor and comfortable recovery; the surgeon wants a nonexplosive agent which effects complete muscular relaxation and does not increase the capillary bleeding; the anesthetist desires a good margin of safety with a minimum of functional or organic injury, adequate potency for high oxygen mixtures and elimination of the unchanged chemical and "moment to moment" control of the depth of anesthesia resulting from rapid interchange of this gas between the atmosphere and the tissues; and the manufacturer hopes for an agent which can be produced simply and inexpensively, is easily purified and remains chemically unchanged during storage.

There is no known gas which meets all the requirements specified, but the experimental and clinical evidence for cyclopropane is considered herewith on the basis of these standards set by Seevers and Waters. Lucas and Henderson [3] introduced cyclopropane for clinical use in 1929 after a preliminary pharmacologic study. Later a preliminary report of 447 clinical cases was published by Stiles, Neff, Rovenstine and Waters [4] in 1934. Other early workers included Griffith,[5] Bourne [6] and Wood.[7] A complete bibliography to date would include more than a hundred references to the use of this agent. The following information is designed to include the pertinent contributions of the many authors who have published reports on this anesthetic gas.

CHEMICAL AND PHYSICAL PROPERTIES

Cyclopropane (C_3H_6), described by von Freund [8] as trimethylene in 1882, is a colorless gas with a characteristic, not unpleasant odor. Its molecular weight is 42.1; its density at 0 C. and 760 mm. of mercury is 1.46. The boiling point of cyclopropane is —32.89 C.[8a] and the freezing point —126 C. [Unpublished data from the laboratories of the Ohio Chemical & Manufacturing Co., Cleveland, Ohio, indicate a boiling point of —32.2 C., and a freezing point of —127 C. for cyclopropane.] It is inflammable and explosive.[9] The lower limits of explosibility are the same as for ether, but the upper limits are much less.[10] The range in air of explosibility is from 3 to 8.5 per cent and in oxygen from 2.5 to 50 per cent.[11] The olive oil to water solubility of an impure cyclopropane gas is 64.4 to 1 as compared with 13.2 to 1 for ethylene and 25.5 to 1 for ether.[3] The oil-water coefficient of pure cyclopropane at 37.5 C. is 34.3.[12] Many authors have reported on its solubility [13] in water, in blood (both human and animal), in various oils by saturation and extraction and in iodine pentoxide. According to Orcutt and Seevers,[12] who used the extraction method, it has at body temperature a solubility in water of about 20.4 volumes per cent and in human oxalated blood 45.7 volumes per cent. The solubility in cod liver oil and paraffin oils is approximately the same as for olive oil, which is 699.0 volumes per cent. According to Robbins,[14] its solubility in blood varies with changes in cell volume as well as in the lipoid content of the blood and, therefore, is increased after a fat meal.

PREPARATION OF VARIOUS BRANDS

The Ohio Chemical & Manufacturing Co. presented its brand of cyclopropane to the Council three years ago. Presumably this product, as well as two other brands—E. R. Squibb & Sons and Imperial Chemical Industries, Ltd.—is manufactured after the method of von Freund.[8] Subsequently, Haas [15] described a new method of preparing the chemical. This method was

1. Cyclopropane for Anesthesia (Ohio Chemical & Manufacturing Co.), Preliminary Report by the Council on Pharmacy and Chemistry, J. A. M. A. **106:** 292 (Jan. 25) 1936.
2. Seevers, M. H., and Waters, R. M.: Pharmacology of the Anesthetic Gases, Physiol. Rev. **18:** 447 (July) 1938.
3. Lucas, G. H. W., and Henderson, V. E.: New Anesthetic Gas: Cyclopropane, Canad. M. A. J. **21:** 173 (Aug.) 1929. Henderson and Lucas: Cyclopropane: A New Anesthetic, Anesth. & Analg. **9:** 1 (Jan.-Feb.) 1930. Lucas and Henderson: Effect of Cyclopropane on Metabolism, Arch. internat. de pharmacodyn. et de therap. **37:** (II): 155, 1930.
4. Stiles, J. A.; Neff, W. B.; Rovenstine, E. A., and Waters, R. M.: Cyclopropane as an Anesthetic Agent, Anesth. & Analg. **13:** 56 (March-April) 1934.
5. Griffith, H. R.: Cyclopropane Anesthesia, Canad. M. A. J. **31:** 157 (Aug.) 1934.
6. Bourne, Wesley: Cyclopropane Anesthesia in Obstetrics, Lancet **2:** 20 (July 7) 1934.
7. Wood, P. M.: Clinical Use of Cyclopropane and Tribromethanol in Amylene Hydrate, J. A. M. A. **106:** 275 (Jan. 25) 1936.
8. von Freund, August: Ueber Trimethylene, Monatsh. f. Chemie **3:** 625 (July 13) 1882.
8a. Hass, H. B.; McBee, E. T.; Hinds, G. E., and Gluesenkamp, E. W.: Synthesis of Cyclopropane, Ind. & Eng. Chem. **28:** 1178 (Oct.) 1936.
9. Sise, L. F.: Anesthesia for Thyroid Surgery, J. Indiana M. A. **30:** 180 (April 1) 1937.
10. Sise, L. F.; Woodbridge, P. D., and Eversole, U. H.: Cyclopropane—A New and Valuable Gas Anesthetic, New England J. Med. **213:** 303 (Aug. 15) 1935.
11. Buchman, M. A., and Wardell, C. H.: The Inflammability of Anesthetic Gases and Vapors Including Cyclopropane, the Ohio Chemical & Manufacturing Co., Cleveland.
12. Orcutt, F. S., and Seevers, M. H.: The Solubility Coefficient of Cyclopropane for Water, Oils and Human Blood, J. Pharmacol. & Exper. Therap. **59:** 206 (Feb.) 1937.
13. Kochmann: Heffter's Handbuch der experimentelle Pharmakologie, Berlin, Julius Springer, 1936, vol. 2. Orcutt and Seevers.[12] Robbins.[14]
14. Robbins, B. H.: Studies on Cyclopropane: I. The Quantitative Determination of Cyclopropane in Air, Water and Blood by Means of Iodine Pentoxide, J. Pharmacol. & Exper. Therap. **58:** 243 (Nov.) 1936.
15. Haas, H. B.; McBee, E. T.; Hinds, G. E., and Gluesenkamp, E. W.: New Method for Preparing Anesthetic Cyclopropane, Anesth. & Analg. **16:** 31 (Jan.-Feb.) 1937.

patented by Purdue University and subsequently sold to the Mallinckrodt Chemical Works, makers of the latest and third American brand.

IMPURITIES

Burger [16] studied the impurities in all three American brands, referring to them as brands *A, B* and *C*. He logically predetermined the likely impurities and noted that the manufacture of the gas required ring closure (ringschluss) and that the "chloride" method was apt to result in the formation of propylene. Wolkow and Menschutkin [17] had noted this previously and Wilstaetter and Bruce [18] had described methods for eliminating propylene. Ipatjew [19] changed 50 to 70 per cent cyclopropane to propylene by passing it over iron filings at 100 C. Burger believed that not only propylene but cyclohexane was likely to be present. It is difficult to detect either, since the two have the same composition (the same empiric but not the same structural formula) as cyclopropane. Burger employed the Wagner [20] cold permanganate method and the Gustavson [21] iodine absorption procedure and found that by the former, brand *A* contained 2.85 per cent propylene, brand *B* 2.56 per cent and brand *C* 0.12 per cent. Results by the latter method checked closely—brand *A* contained 2.80 per cent, *B* 2.50 per cent and *C* 0.14 per cent of propylene. Burger did not claim that these tests were positive but merely that propylene was the most likely compound to give positive results of these tests. He could devise no test for the presence of cyclohexane but was suspicious of its presence because of the similarity of odor to that of chloroform, even though the test for haloids was negative. In his opinion cyclohexane was more undesirable than propylene, but he also believed that it could be eliminated by careful fractional distillation. Buchman and Wardell [11] have stated that propylene, propane, higher hydrocarbons, ethers, alcohols, alkyl halides and nitrogen are the impurities which are most likely to be encountered in cyclopropane.

CONCENTRATION, SATURATION AND DIFFUSION

Cyclopropane differs from other gaseous anesthetic agents in that the anesthetic-oxygen ratio is reversed—15 per cent of cyclopropane to 85 per cent of oxygen up to the rarely and briefly used 40 per cent of cyclopropane and 60 per cent of oxygen.[22] Robbins [23] found in seventeen dogs that abdominal relaxation required 16.8 mg. per hundred cubic centimeters of blood, that loss of the wink or lid reflex required 20.6 mg. in 100 cc., and that costal paralysis ensued when 25.5 mg. of the anesthetic was present and respiratory arrest occurred when 100 cc. contained 28.2 mg. of cyclopropane. Seevers notes that this gas possesses analgesic properties in subanesthetic concentrations of from 3 to 5 per cent if continuously inhaled.[24] Most normal persons will lose consciousness following prolonged inhalation of 6 per cent or less, although effective concentrations vary widely with the person.[24]

Romberger [25] points out, however, that nothing could be farther from reasonable physiologic truth than that set percentage mixtures of cyclopropane-oxygen are indicative of definite places or levels of anesthesia. Furthermore, he points out that the exact percentages are indeterminate unless minute to minute samples are taken. He concludes that since the use of ether and the open mask gives no index of percentages, it is necessary to use signs; the same index should be used with cyclopropane.

Barbour [26] stated that "the amount taken up by the blood is directly proportional to the partial pressure of the gas existing in the alveolar air and to the solubility coefficient for that particular anesthetic." According to Robbins,[27] blood cells absorb about two and one-half times as much cyclopropane as blood plasma. He found the distribution coefficient (blood concentration/air concentration) in the dog to be 0.492 in vivo and 0.513 in vitro—a good agreement. Concentration of cyclopropane in the blood of the right side of the heart is practically equal to that in the arterial blood after fifteen minutes of anesthesia.[27] That complete body saturation does not occur at this time (but several hours later), is indicated by Seevers' data [28] on the dog and rabbit by the gas depot method. Similar data have been obtained on man by the same method.[29] Appreciable quantities of the gas are lost to the tissues throughout an ordinary anesthesia.[30]

When the pressure gradients are diminished as saturation or desaturation is approached, the diffusion rate is much prolonged, as indicated by Robbins' data showing that the venous blood still retained some cyclopropane after from two to three hours of cyclopropane. The rate of diffusion of cyclopropane appears to be about twice that of ethylene.[31] That ethylene is eliminated more rapidly than cyclopropane may be inferred from the difference in potency and the fact that induction and recovery are slower with the latter agent. Romberger, using Ronzoni's [32] data for ether, found that cyclopropane was eliminated much faster than ether.

PHARMACOLOGIC EFFECTS

Heart and Circulation.—Waters notes that the entire effect of this agent on the vascular system, coronary vessels and myocardium is not established, but nevertheless certain facts are available. Waters and his associates [33] and Sise [10] have both warned that if bradycardia, arrhythmias or tachycardia developed during cyclopropane anesthesia the concentration must be lessened at once. Lucas, Henderson and Waters noted that high concentrations of cyclopropane produced cardiac arrhythmia in experimental work on animals and man. Seevers and his associates [34] observed these arrhythmias just prior to or following respiratory arrest in concentrations of over 35 per cent in dogs. Robbins and Baxter [35] concluded that the arrhythmias occurring after respiratory arrest in the dog are due to anoxemia and not to cyclopropane per se, since they occurred when the arterial blood contained only 2.8 per cent oxygen, and that vagal section did not prevent them, although it did prevent the increase in the PR interval and the more severe type of auriculoventricular block which occurs earlier in anesthesia. Seevers and his associates thought that early arrhythmia was of vagal origin, since it was prevented by atropine and was not entirely due to anoxemia, even though this was a factor and plays a major role in the arrhythmia occurring later. Waters [30] studied the incidence of arrhythmia clinically and found that it increased with deepening cyclopropane anesthesia and lessened with deepening ether anesthesia. Kurtz, Bennett and Shapiro [36] encountered four cases of multiple focus ventricular tachycardia in a series of forty-one clinical administrations purposely carried to the

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17. Wolkow, A., and Menschutkin, B. N.: Ber. d. deutsch. chem. Gesellsch. **31:** 3070, 1898.
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19. Ipatjew, W.: Ber. d. deutsch. chem. Gesellsch. **35:** 1063, 1902.
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21. Gustavson, G.: J. prakt. Chem. (2) **62:** 285, 1900. Gustavson, G.: J. prakt. Chem. (2) **62:** 294, 1900.
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24. Seevers, M. H.; Bennett, J. H.; Pohle, H. W., and Reinardy, E. W.: The Analgesia Produced by Nitrous Oxide, Ethylene and Cyclopropane in the Normal Subject, J. Pharmacol. & Exper. Therap. **59:** 291 (March) 1937.
25. Romberger, F. T.: Cyclopropane: A Teaching View Point, Anesth. & Analg. **17:** 118 (March-April) 1938.
26. Barbour, H. G.: Pharmacological Action of Inhalation Anesthetics, Am. J. Surg. **34:** 435 (Dec.) 1936.
27. Robbins, B. H.: Quantitating Cyclopropane in Air and Blood, Anesth. & Analg. **16:** 93 (March-April) 1937.
28. Seevers, M. H.; DeFazio, S. F., and Evans, S. M.: A Comparative Study of Cyclopropane and Ethylene with Reference to Body Saturation and Desaturation, J. Pharmacol. & Exper. Therap. **53:** 90 (Jan.) 1935.
29. Seevers, Stormont and Hathaway: Unpublished experiments.
30. Waters, R. M.: Present Status of Cyclopropane, Brit. M. J. **2:** 1013 (Nov. 21) 1936.
31. Seevers, M. H.; DeFazio, S. F., and Evans, S. M.: Comparative Study of Cyclopropane and Ethylene with Reference to Body Saturation and Desaturation, J. Pharmacol. & Exper. Therap. **53:** 295 (March) 1935.
32. Ronzoni, E.: J. Biol. Chem. **57:** 761 (Oct.) 1923.
33. Waters, R. M., and Schmidt, E. R.: Cyclopropane Anesthesia, J. A. M. A. **103:** 975 (Sept. 29) 1934. Waters,[30] Seevers, Meek, Rovenstine and Stiles.[34] Kurtz, Bennett and Shapiro.[36]
34. Seevers, M. H.; Meek, W. J.; Rovenstine, E. A., and Stiles, J. A.: A Study of Cyclopropane Anesthesia with Especial Reference to Gas Concentrations, Respiratory and Electrocardiographic Changes, J. Pharmacol. & Exper. Therap. **51:** 1 (May) 1934.
35. Robbins, B. H., and Baxter, J. H., Jr.: Studies on Cyclopropane: III. The Relation of Electrocardiographic Changes to the Arterial Concentrations of Oxygen, Carbon Dioxide and Cyclopropane in Dogs Anesthetized with Cyclopropane, J. Pharmacol. & Exper. Therap. **61:** 162 (Oct.) 1937.
36. Kurtz, C. M.; Bennett, J. H., and Shapiro, H. H.: Electrocardiographic Studies During Surgical Anesthesia, J. A. M. A. **106:** 434 (Feb. 8) 1936.

fourth plane, which indicates, as do certain animal experiments, that since the irregularities are of ventricular origin there is increased irritability of the automatic tissue of the heart. The work of Moffitt[37] indicates that bradycardia occurred most frequently with cyclopropane majors followed in order by ethylene minors, ether majors and nitrous oxide majors.

Eversole[38] studied cardiac irregularities in 109 patients receiving 113 anesthesias and encountered cardiac irregularities in 79 per cent of the cyclopropane cases; 90 per cent of the ether cases and 100 per cent of the chloroform cases. The disturbances were frequently pacemaker displacement or sinus arrhythmias. Thirty-one of the group had cardiac irregularities preoperatively. Tachycardia occurred in four of the cyclopropane cases. Marshall[39] believed that arrhythmia, bradycardia, and tachycardia were closely related to increased concentrations. In 7,200 administrations with which Waters was familiar there were three deaths, one of which was a preanesthetic circulatory failure and the other two were probably due to ventricular fibrillation. They were attributed to technical errors of administration, for although fine concentrations were used for induction it was increased rapidly through respiratory depression. Simmons[40] reported one death in ventricular fibrillation.

Some interesting light is thrown on the subject of the relationship of cyclopropane to these rare disturbances by the use of epinephrine during anesthesia. Meek and his associates[41] concluded from their experiments that cyclopropane affects the automatic tissue of the heart in dogs to a greater extent than ether or chloroform. They state in part:

"In the adrenalin controls A-V blocks were common and the ventricular rhythms were slow in nature. When the heart was under the influence of cyclopropane, however, the ventricular specialized tissue was so heightened in its irritability that when adrenalin reached it an automatic rate appeared that was dominant over the sinus. The ventricular tachycardias were almost always at the rate of 300 a minute."

They[41] also showed that the predisposing effect of cyclopropane for ventricular tachycardia seemed to be directly related to the concentration of the anesthetic agent. With epinephrine tachycardia developed in fewer animals under light anesthesia than under deep. Even more significant than the numerical occurrence of the tachycardia was the length to which it persisted. Under light cyclopropane, the tachycardia lasted less than half as long as under deep anesthesia.

The significance of these observations, however, is difficult to evaluate from a practical standpoint, in the opinion of Seevers and Waters,[2] since irregularities are a common clinical occurrence with all types of anesthesia including procaine blocks. In Kurtz's series,[36] of 109 cases with all agents, only 21 per cent failed to show some disturbance of cardiac rhythm.

Cyclopropane in anesthetic concentrations relaxes the peripheral blood vessels, according to Seevers and Waters,[2] and venous blood becomes arterialized even when the inspired oxygen is 21 per cent. Capillary bleeding seems to be increased;[2] according to Marshall,[39] this is due in part to the absence of compensatory sympathicotonia and hyperadrenia.

The blood pressure may rise during cyclopropane anesthesia, and this is believed to be due to the accompanying retention of carbon dioxide, anoxemia or pressor reflexes which rise from the sensory stimulation of light anesthesia rather than from the anesthetic agent per se, since if care is taken to eliminate these factors a rise is seldom seen. Rowbotham[42] found that systolic blood pressure was increased 10, 20 and 30 mm. at the start of anesthesia and that this rise was followed by a rise in the diastolic, both rises in his opinion being proportional to the depth of anesthesia. Contrarily, he used anesthesia in a case of hypertension in which there was no change in the blood pressure. Moffitt[37] noted lowering of blood pressure with nitrous oxide majors, cyclopropane minors and ethylene majors in the order of incidence. Sise[10] states that the blood pressure drops or rises slightly in cyclopropane anesthesia and Bogan[43] claimed a rise of blood pressure of from 10 to 20 mg.

Experimental and clinical evidence indicates that electrocardiographic change encountered during cyclopropane anesthesia is transient rather than permanent, but there are as yet no functional or pathologic studies determining definitely the absence of permanent effects. Tucker[44] reported one case of shock in a patient who had received 750 cc. of cyclopropane. The patient recovered, but Tucker recommended watching closely for shock and poor operative risks. Moffitt[37] did not believe that there was any great difference in the circulatory depression seen in cyclopropane as compared with those following nitrous oxide-ether anesthesia. As a matter of fact, he found shock more frequent in both nitrous oxide majors and ether majors than he did in cyclopropane majors. Although the early experimental work on dogs and man indicated that the heart rate is usually reduced below the resting level[45] Waters does not believe that further work will confirm this finding.

In the opinion of Romberger,[22] untoward effects on the heart in the cardiovascular system should not occur under reasonably normal circumstances. Sanders[46] believes that cyclopropane is less dangerous to the heart than other agents, and Marshall postulates that apart from minor disturbances of rate and rhythm in deep anesthesia cyclopropane has little toxicity for the circulatory system, since he believes that the compensatory sympathicotonia and hyperadrenia of ether and chloroform are absent.

It can be definitely stated, however, that deep concentrations of cyclopropane are inexcusable, both because they are unnecessary and because they are potentially dangerous to cardiac tissue. The combination of epinephrine and other sympathicotonic drugs or any drugs that increase the irregularities of the automatic tissue of the heart should be avoided. It is essential to watch the pulse carefully and continually during cyclopropane anesthesia, especially if anesthesia is deepened to the point of beginning respiratory depression.[47] Sise notes that high concentrations are toxic to the heart but that they should never be used clinically, while Waters warns that rapid induction should be avoided. Waters and his associates are continuing their studies of the effects of cyclopropane on the cardiovascular rhythm as well as of cardiac damage and other circulatory effects.

Robbins and Baxter[48] found in dogs that cardiac output was increased under surgical anesthesia and remained unchanged or was decreased under very deep anesthesia.

Respiratory System.—Cyclopropane is an anesthetic gas which has a characteristic, not unpleasant odor and which, according to Romberger,[22] is practically nonirritating in concentrations less than 50 per cent used clinically.[10] The Imperial Chemical Industries, Ltd., brand is claimed by the Englishman Rowbotham[42] to be less pungent and more pleasant to breathe than the Ohio Chemical & Manufacturing Co. brand.

Waters[30] points out that the irritant property of ether vapor precludes the temptation to use high concentrations, while cyclopropane is devoid of that irritation. Because of this and the abundant oxygen present, there is little to discourage the careless anesthetist from using too much of this potent anesthetic agent. Authorities differ as to whether laryngospasm is more frequent or less frequent with cyclopropane than with other anesthetic agents. The respiratory stimulation so commonly seen in the initial and lighter stages of ether anesthesia is absent in cyclopropane except when preliminary medication is also employed or there is accumulation of carbon dioxide in the closed system.[22] Other factors contributing to the ease with which this agent may be administered without indication of dangerous

37. Moffitt, J. A., and Mechling, G. S.: A Comparison of Cyclopropane with Other Anesthetics, Anesth. & Analg. **15**: 245 (Sept.-Oct.) 1936.
38. Eversole, U. H.; Sise, L. F., and Woodbridge, P. D.: Clinical Use of Cyclopropane, Surg., Gynec. & Obst. **64**: 156 (Feb. 1) 1937.
39. Marshall, S. V.: Cyclopropane Anesthesia: A Preliminary Survey, M. J. Australia **2**: 138 (July 24) 1937.
40. Simmons, H. J. A., in discussion on paper by Waters.[30]
41. Meek, W. J.; Hathaway, Hubert, and Orth, O. S.: The Effects of Ether, Chloroform and Cyclopropane on Cardiac Automaticity, J. Pharmacol. & Exper. Therap. **61**: 240 (Nov.) 1937.
42. Rowbotham, Stanley: Cyclopropane Anesthesia, Lancet **2**: 1110 (Nov. 16) 1935.
43. Bogan, J. B.: A Clinical Evaluation of Cyclopropane After Its Use in 300 Surgical Anesthesias, Anesth. & Analg. **15**: 275 (Nov.-Dec.) 1936.
44. Tucker, E. B.: Observation on the Use of the Newer Anesthetics: Vinethene and Cyclopropane, Anesth. & Analg. **16**: 55 (Jan.-Feb.) 1937.
45. Seevers and Waters.[2] Seevers, Meek, Rovenstine and Stiles.[34] Bogan.[43]
46. Sanders, R. L., and Fink, J. C.: Cyclopropane Anesthesia; Clinical Observations in 100 Cases, Memphis M. J. **11**: 8 (Aug.) 1936.
47. Waters.[30] Sise, Woodbridge and Eversole.[10]
48. Robbins, B. H., and Baxter, J. H., Jr.: Studies of Cyclopropane: IV. Cardiac Output in Dogs Under Cyclopropane Anesthesia, J. Pharmacol. & Exper. Therap. **62**: 179 (Feb.) 1938.

concentration is the smooth induction, which usually occurs without excitement, and the fact that it is essentially a respiratory depressant, especially when premedication is employed.

Waters [30] made a thorough study of the effect on the respiratory system and found that there was no stimulation during inhalation, slight depression during the first and second planes and very slight depression in the third plane down to the point at which respiratory arrest began to approach. In this respect it differs from all other anesthetic gases.[49] Even the increasing rate, which usually occurs with other agents just prior to respiratory arrest, is very slight or absent. The decrease in minute-volume respiration is accompanied by an increase in the carbon dioxide content in the arterial blood [30] and the tissues.[28] Bourne has been reported to have suggested that the oxygen-rich atmosphere used with cyclopropane may be responsible for the retention of carbon dioxide by the muscles and other tissues and that this carbon dioxide toxicity may be responsible for the postoperative collapse seen occasionally with this anesthetic. In increasing concentrations to the point of respiratory arrest, it is seen that respiration invariably fails before circulation and, therefore, that recovery occurs readily if artificial respiration is instituted and the concentration diminished.

Moffitt [37] in his studies of various anesthetics noted the incidence of pharyngitis decreasing in the following order: ethylene majors, ethylene minors, nitrous oxide majors and cyclopropane majors, but on the other hand cough was most frequent in cyclopropane majors and ethylene majors. Pneumonias occurred most frequently in nitrous oxide majors; nausea in ethylene minors and emesis in ether majors, ether minors and ethylene majors in order. The early work reported on the lowered incidence of pulmonary complication in anesthesia with this agent by the Wisconsin workers has been confirmed by Bonham.[50] Knight and Urner [51] did not encounter any respiratory complications in thirty-two cases in which they used cyclopropane in a self-administering device for obstetric analgesia. However, pulmonary complications are not common in obstetric analgesia and anesthesia.

Mechling and Moffitt [52] found the incidence of pneumonia increased in the following order: spinal, nitrous oxide, cyclopropane, ether and ethylene; for bronchitis and pharyngitis ethylene, cyclopropane, nitrous oxide, spinal and ether.

The clinical anesthesia results in relatively slight salivation. Waters believes that it is much less than that obtained with ether and chloroform and more than that obtained with nitrous oxide and ethylene. Seevers and Waters note that little is known concerning the secretion of mucus resulting from these various anesthetic agents and that the mucus rather than the serous secretion is more troublesome during anesthesia.

Burford [53] reported an incidence of 0.97 per cent of pulmonary complications in his series of 1,333 administrations and noted that Taylor and his associates [54] reported an incidence of 0.95 per cent in a series of 5,889 administrations. Griffith,[55] in a series of 300 cases, reported pulmonary complications of 0.67 per cent while Moffitt and Mechling [56] reported none in 315 cases.

Burford,[53] however, had a pulmonary complication incidence of 2.07 per cent in his 626 abdominal cases and Griffith [55] 1.8 per cent in 109 abdominal cases. Burford and Jones [57] reported four deaths due to massive atelectasis and discussed their possible cause—quiet respiration and high alveolar oxygen and prevention by the addition of helium to the anesthetic mixture. Griffith [58] reported a case of acute pulmonary edema following cyclopropane with recovery.

Gastrointestinal Tract.—Raginsky and Bourne [59] found no liver injuries in dogs after repeated [9] daily administrations for periods of one hour, as judged by the capacity to eliminate bromsulphalein and by histologic examination. Neither did cyclopropane have an adverse effect on the rate of recovery from hepatic injury produced by chloroform, as judged by the same criteria. These authors, according to Seevers and Waters, could find no evidence of additional hepatic injury to eclamptic patients who gave evidence of such injuries by retention of dye.

Peoples and Phatak [60] reported an increased tone of isolated rabbit jejunum when exposed to from 10 to 25 per cent cyclopropane in oxygen. Meek's associates Weisel, Youmans and Cassels [61] have found that both the circular contractions and propulsive phenomena are inhibited or arrested in normal dogs with Thiry or Thiry-Vella fistulas during deep cyclopropane anesthesia. Prompt return to normal or increased activity occurred when anesthesia was terminated. Peoples and Phatak [60] believed that these results indicated that there would probably be less postoperative intestinal stasis and distention in the clinical use of cyclopropane than there was with ether. Seevers [62] observed that the ten minute inhalation of 6 per cent cyclopropane inhibited hunger contractions in man without affecting gastric tone. These contractions returned in full strength when inhalation ceased and progressed to the usual tetanic contracture.

Waters reports that in a series of 10,638 cases, nausea and vomiting occurred in 56.5 per cent of the ether cases; 39 per cent of the cyclopropane cases; 33 per cent of the ethylene cases, and 23 per cent of the nitrous oxide cases.

Mechling and Moffitt [52] found the incidence of nausea and vomiting to decrease in the following order: ether, ethylene, cyclopropane, nitrous oxide and spinal anesthesia. Romberger [22] believed that cyclopropane-oxygen compares favorably with ethylene-oxygen as far as the incidence of postoperative nausea and vomiting are concerned. Gould [63] noted postoperative nausea.

Tucker,[44] Morgan,[64] Griffith [65] Knight and Urner [51] and Romberger [22] noted that nausea and vomiting were lessened with cyclopropane, especially if there had been premedication, and that cyclopropane produces less nausea and vomiting than ether but more than nitrous oxide.

In the series of 10,638 cases referred to, distention occurred in 16⅔ per cent of the 2,400 ether cases; 13 per cent of the 5,800 cyclopropane cases; 7 per cent of the 1,000 ethylene cases, and 3 per cent of the 1,300 nitrous oxide-oxygen cases. In this series nitrous oxide or ethylene were seldom used for abdominal operations or the incidence of distention with these agents would have been higher. Morgan [64] and Griffith [65] encountered less distention than with other agents.

Genito-Urinary Tract.—Burger [16] notes that the effect of cyclopropane on kidney function and bladder musculature remains to be studied, but Sanders and Fink [46] pointed out that Waters and Schmidt noted that the kidney output was occasionally depressed during cyclopropane anesthesia and that it was followed by a compensatory increase several hours later such as occurs with ether and ethylene. They [46] believed that bladder function was less affected, since fewer catheterizations were required following cyclopropane anesthesia. They [46] also believed that distention was reduced and diminished.

Waters gives the incidence of urinary retention in his series as 7.5 per cent of cyclopropane cases, 5.4 per cent of ether, 2 per cent of ethylene and 2.8 per cent of nitrous oxide. In general, however, he believes that retentions are not related to the anesthetic per se but rather to the type of operation performed. Mechling and Moffitt [52] found the incidence of reten-

49. Seevers, Meek, Rovenstine and Stiles.[34] Waters.[30]
50. Bonham, R. F.: Cyclopropane Anesthesia, Texas State J. Med. **33:** 306 (Aug.) 1937.
51. Knight, R. T., and Urner, J. A.: Obstetrical Analgesia, Journal-Lancet **56:** 608 (Dec.) 1936.
52. Mechling, G. S., and Moffitt, J. A.: Cyclopropane in Comparison with Other Anesthetic Agents, J. Oklahoma M. A. **29:** 204 (June) 1936.
53. Burford, G. E.: Pulmonary Complications Following 1,333 Administrations of Cyclopropane, J. A. M. A. **110:** 1087 (April) 1938.
54. Taylor, I. B.; Bennett, J. H., and Waters, R. M.: Anesthesia at the Wisconsin General Hospital: Anesthesia Methods and Postoperative Respiratory Complications, Anesth. & Analg. **16:** 198 (July-Aug.) 1937.
55. Griffith, H. R.: Cyclopropane Anesthesia, Anesth. & Analg. **14:** 253 (Nov.-Dec.) 1935.
56. Moffitt, J. A., and Mechling, G. S.: A Comparison of Cyclopropane with Other Anesthetics, Anesth. & Analg. **15:** 225 (Sept.-Oct.) 1936.
57. Jones, O. R., and Burford, G. E.: Massive Atelectasis Following Cyclopropane Anesthesia, J. A. M. A. **110:** 1092 (April 2) 1938.
58. Griffith, H. R.: Two Unusual Complications in Patients Under Cyclopropane Anesthesia, Anesth. & Analg. **17:** 298 (Sept.-Oct.) 1938.
59. Raginsky, B. B., and Bourne, Wesley: Effects of Cyclopropane on the Normal and Impaired Liver, Canad. M. A. J. **31:** 500 (Nov.) 1934.
60. Peoples, S. A., and Phatak, N. M.: Effect of Cyclopropane on Isolated Intestinal Muscle, Proc. Soc. Exper. Biol. & Med. **33:** 287 (Nov.) 1935.
61. Weisel, Wilson; Youmans, W. B., and Cassels, W. H.: Effect on Intestinal Motility of Cyclopropane Anesthesia Alone and After Morphine-Scopolamine Premedication, J. Pharmacol. & Exper. Therap. **63:** 391 (Aug.) 1938.
62. Seevers: Unpublished experiments.
63. Gould, R. B., in discussion on paper by Waters.[30]
64. Morgan, G. S.; Eaman, S. G., and Griffith, H. R.: Cyclopropane Anesthesia for Cesarean Section, Anesth. & Analg. **16:** 113 (March-April) 1937.
65. Griffith, H. R.: Cyclopropane Anesthesia, Anesth. & Analg. **14:** 253 (Nov.-Dec.) 1935.

tion to increase in the following order: spinal, cyclopropane, nitrous oxide, ethylene and ether. Nephritis occurred most frequently in nitrous oxide majors, ether majors and cyclopropane majors, in that order.[37]

Central Nervous System.—Tucker [44] reported a few cases of headache with cyclopropane and one case in which there was no headache with ethylene. Knight and Urner [51] found no mental dulness following prolonged administrations. Challis [66] complained that headache was encountered in those occupying the amphitheater during cyclopropane anesthesia. Mechling and Moffitt [52] found that the incidence of headache decreased in the following order: spinal, cyclopropane, nitrous oxide, ethylene and ether. Griffith [58] reported a case of convulsions under cyclopropane and nupercaine, apparently due to an idiosyncrasy to the nupercaine.

Other Pharmacologic Effects.—Henderson and Lucas noted but little rise in the blood sugar of cats and rabbits during cyclopropane anesthesia. Eversole [38] notes that there is a temporary slight rise in blood sugar but no change in the acid base balance. Henderson and Lucas found that there was little effect on the hydrogen ion concentration and carbon dioxide combining power of the blood. Seevers and Waters note that there is a 10 per cent rise in blood sugar. A 75 per cent elevation in blood phosphorus occurred. According to Seevers and Waters, Neff and Stiles [67] observed an 8 to 30 per cent rise in the blood sugar of twenty-five patients. Schmidt and Waters noted that the nonprotein nitrogen and carbon dioxide combining power of blood were not significantly affected in twenty-one clinical administrations. There was a constant lowering of carbon dioxide combining power by from 2 to 7 volumes per cent but no change in the nonprotein nitrogen. They did not observe any change in the carbon dioxide combining power of thirty controlled diabetic patients anesthetized with cyclopropane.

Taylor and Waters [68] found that cyclopropane like other agents—nitrous oxide, ethylene and ether—produced an absolute and relative increase of the leukocytes of peripheral blood which persisted several days after anesthesia. That this rise was not due to trauma was indicated by the fact that unoperated dogs show slight changes. No consistent changes in red cell volume or coagulation time were reported by Seevers and Waters.[2]

There is no evidence that cyclopropane undergoes any chemical alteration in the body or that it is isomerized to propylene [28] (see under impurities). There is no clear-cut histologic evidence of parenchymatous injury by cyclopropane, but the question is not settled, particularly in view of the evidence of functional alteration of cardiac automaticity.[2] Such a study is desirable, but in order to be convincing the evidence must be obtained on animals living under controlled dietary conditions.

CLINICAL ANESTHETIZATIONS

Signs of Anesthesia.—One of the most important points to consider in the administration of cyclopropane is that it is not a respiratory stimulant. Of equal importance is the fact that the color of the patient cannot be used as an index of the plane or depth of anesthesia. It is Bonham's opinion [50] that the pulse gives the best index of the patient's condition and that either a marked slowing to 50 or a definite increase indicates overdosage. The signs of Guedel [69] are not applicable to anesthesia under cyclopropane. Romberger made a special study of the signs of the various planes of cyclopropane anesthesia. The first sign to observe according to his plan is the lid reflex. It gradually lessens during induction and becomes absent when the patient enters early sleep. This is the first plane of anesthesia and, according to Waters and Schmidt,[70] represents a concentration of about 7.4 per cent. Romberger's index for the second plane of anesthesia is the eyeball movement, which lessens as anesthesia develops and serves as an index of the depth of anesthesia during the second plane which, according to Schmidt and Waters, occurs approximately at 13.1 per cent concentration. The third plane begins when the movement of the eyeball ceases and thereafter deep anesthesia is being approached rapidly and caution is necessary. The concentration at this point of the anesthesia ranges around 23.3 per cent, according to Schmidt and Waters. Anesthesia is maintained at the desired level—somewhere in the second plane—by cutting off the cyclopropane and continuing the oxygen until the depth is lessened. In deep anesthesia—third plane—the respiratory rate and amplitude is the only safe sign to follow, according to Romberger,[22] and it is quick. To maintain anesthesia it may be necessary to supply a trickle of cyclopropane (from 25 to 100 cc. per minute) for from six to ten minutes to compensate for leakage, diffusion and usage. There is no cyanosis with cyclopropane oxygen anesthesia, and it should never be permitted to ensue and hence is not a practical sign of the depth of anesthesia. When it does occur in cyclopropane anesthesia it indicates anoxemia with excessive carbon dioxide.

Passage through the first two stages described is usually very rapid and, as noted, the ordinary signs of anesthesia are missing. There is always a potential danger unless proper caution is used of encountering overdosage, which along with high concentrations and accumulated effects produces a fall in the rate of respiration and a lessening in tidal exchange. Both of these are indicated by the excursions of a breathing bag, and it is important to note that they may occur even in the presence of a very pink color of the patient.

ADMINISTRATION METHODS

Of primary consideration in the administration of this anesthetic is the fact that it is an explosive agent. For this as well as for other reasons the closed technic is preferable. Waters has stated that the carbon dioxide absorption setup attached to a completely closed machine was the best safeguard against explosion, but that, nevertheless, cyclopropane must always be considered to have the same potential danger as ether and ethylene. Bonham,[50] using this technic, starts with a bag two-thirds full of oxygen and permits a flow of cyclopropane and oxygen, each 500 cc. per minute for from three to five minutes. He then temporarily discontinues the cyclopropane, allowing the patient to breathe the mixture in the bag. He adds it gradually in small amounts as needed. Griffith [65] fills the bag with oxygen and then adds cyclopropane at the rate of from 500 to 600 cc. per minute until anesthesia is established and then maintains it at the required plane with a mixture of oxygen and cyclopropane.

Romberger fills the bag partly or completely with oxygen and then permits the patient to breathe into the closed circuit, at which time a small stream of cyclopropane is started, ranging from 250 to 750 cc. per minute. Anesthesia is maintained at the desired level, as indicated by the signs and not by estimates of percentages,[25] by cutting off the cyclopropane and continuing the oxygen, supplying as necessary a trickle of cyclopropane from 25 to 100 cc. per minute for from six to ten minutes to compensate for leakage, diffusion and usage.

Sise, Woodbridge and Eversole fill the breathing bag with sufficient oxygen for tidal breathing, place a mask on the face and increase the flow of anesthetic to from 200 to 300 cc. per minute until the loss of the lid reflex, when it is reduced to one third this amount or discontinued; the remainder of anesthesia consists of basal oxygen with occasional additions of cyclopropane necessary to maintain anesthesia.

PREMEDICATION

The addition of various agents used in premedication must be carefully considered when cyclopropane anesthesia is to be employed. The principal reason for precautionary use of such agents is the fact that the gas is not a respiratory stimulant. Sise and his co-workers [10] note that the signs of anesthesia under cyclopropane are much clearer without premedication and are difficult to determine, important as they are, if much premedication has been administered. It has been noted [2] that if premedication is employed lower concentrations of the gas produce satisfactory anesthesia in man. It has been stated that premedication is contraindicated with cyclopropane because it is not a respiratory stimulant, and such medication should be limited to allaying apprehension.

66. Challis, J., in discussion on paper by Waters.[30]
67. Neff, W. B., and Stiles, J. A.: Some Experiences with Cyclopropane as an Anesthetic with Special Reference to the Diabetic Patient, Canad. M. A. J. **35**: 56 (July) 1936.
68. Taylor, I. B., and Waters, R. M.: Leukocytosis Following Inhalation Anesthesia, Anesth. & Analg. **14**: 276 (Nov.-Dec.) 1935.
69. Guedel, A. E.: Stages of Anesthesia and Reclassification of the Signs of Anesthesia, Anesth. & Analg. **6**: 157 (Aug.) 1927.
70. Waters, R. M., and Schmidt, E. R.: Cyclopropane Anesthesia: Postoperative Morbidity in 2,200 Cases, Anesth. & Analg. **14**: 1 (Jan.-Feb.) 1935.

Griffith [65] has used 3 grains (0.2 Gm.) of pentobarbital sodium and 1/150 grain (0.0004 Gm.) of atropine preoperatively but has avoided the use of morphine. Rowbotham,[42] who incidentally encountered many difficulties which at least in part were due to overuse of premedication, employed omnopon (pantopium hydrochloride) 1/30 grain (0.002 Gm.) per stone [71] or pentobarbital sodium intravenously or evipal in addition to pantopium hydrochloride and scopolamine. Mechling and Moffitt [37] recommend premedication with scopolamine but not with the opiates or atropine, while Marshall [39] recommends atropine or scopolamine to restrict salivation.

Sanders and Fink [46] believe that premedication is contraindicated as a general rule but nevertheless use one-sixth grain (0.01 Gm.) of pantopon (pantopium hydrochloride) two hours preoperatively and repeat the dose with the addition of 1/150 grain of atropine sulfate one hour preoperatively. Bonham [50] believes that premedication should be employed cautiously and used 1½ grains (0.1 Gm.) of pentobarbital sodium one and one-half hours preoperatively and pantopon, one-third grain (0.02 Gm.) with atropine, 1/150 grain one-half hour preoperatively. Seevers and Waters determined that the use of ordinary doses of morphine preoperatively reduced by from 10 to 12 per cent the amount of cyclopropane required to effect a given level of anesthesia.

Sise [9] believes that premedication is an individual problem. He uses 3 grains of pentobarbital sodium one and one-half hours preoperatively and the usual one-eighth grain (0.008 Gm.) of morphine sulfate and from 1/200 to 1/250 grain (0.3 to 0.25 mg.) of scopolamine subcutaneously forty-five minutes preoperatively. He believes that premedication is especially valuable in "activated hyperthyroidism," in which he generally employs 4½ grains (0.3 Gm.) of pentobarbital, one-fourth grain (0.016 Gm.) of morphine sulfate and 1/100 grain of scopolamine. On the other hand, in "apathetic hyperthyroidism" he used less than the usual amount of premedication, i. e., one-tenth grain (0.006 Gm.) of morphine sulfate.

INDUCTION, MAINTENANCE AND RECOVERY

Induction with cyclopropane is pleasant, and this fact becomes one more reason for its careful administration. Patients who have been given various anesthetic agents have expressed a preference for cyclopropane. Anesthesia generally ensues in from one to two minutes and, as already noted, premedication has the effect of flattening out each stage of anesthesia.[22] There is generally no choking [52] and seldom any struggling—Bogan's series showed excitement in only 3 per cent.[43] Nevertheless, as Marshall pointed out, it is necessary to allow sufficient time to elapse before surgical procedures are instituted, for otherwise troublesome and sometimes persistent laryngeal spasm occurs, necessitating the introduction of a Magill endotracheal tube for its correction and control.

It is noted under the general discussion of administration methods that, once established, cyclopropane anesthesia is not difficult to maintain. In fact it is sometimes only necessary to replace quantities lost or absorbed. At any rate, the addition of small amounts of cyclopropane to the breathing mixture from time to time, as indicated by the condition of the patient and the plane of anesthesia, produces a satisfactory maintenance. Sise, Woodbridge and Eversole [10] believe that 4 liters of cyclopropane an hour should produce adequate anesthesia for the average case. Marshall [39] noted that 4 or at most 8 liters of cyclopropane should suffice and that oxygen is used at the rate of about 20 liters an hour. Marshall pointed out the advantages of the closed circuit method—definite concentrations of cyclopropane and oxygen were presented to the patient because oxygen is supplied continuously in sufficient amounts to meet the patient's basal requirements, because a carbon dioxide soda-lime absorption device can be thrown in or out of the circuit at will, and finally because the enclosed gases so rapidly become saturated with water vapor that the danger of ignition is reduced and irritation diminished.

Recovery from cyclopropane anesthesia is relatively rapid in spite of the fact that desaturation takes place over a period of several hours, as has been noted. Mechling and Moffitt believe that these patients as a rule are a little slower in recovering than are patients to whom other gases have been administered alone, not in combination with another agent.

71. One stone equals 14 pounds (6.4 Kg.).

RELAXATION AND OOZING

There has been some difficulty with cyclopropane in connection with the degree of abdominal relaxation obtainable at low anesthetic levels. Those who have had the most experience with the agent, however, have not found it necessary to add other ingredients to the anesthetic mixture to obtain satisfactory relaxation. In Romberger's opinion [22] relaxation is less satisfactory than with ether but more satisfactory than with ethylene or nitrous oxide. Marshall [39] believed that relaxation was usually adequate. Sanders and Fink [46] went so far as to state that muscular relaxation was in many cases even better than with ether. It is granted that third plane anesthesia may be required to effect complete abdominal relaxation, but it must be remembered that third plane anesthesia occurs at a concentration of approximately 23 per cent, which still leaves more than 70 per cent of oxygen in the anesthetic mixture. In dogs it was obtainable in concentrations of from 22 to 24 per cent.[14] Griffith was able to obtain adequate relaxation without the addition of ether in 90 per cent of his cases.

Griffith [65] notes that surgeons observed an increased capillary oozing but believes it is more apparent than real because of the bright red color of the blood under cyclopropane anesthesia. He believes also that it is superficial rather than deep because it continues only as long as the tissue is handled.

GAS MACHINES AND SPECIAL DEVICES

Only the most modernly constructed or adapted gas oxygen machines should be used in cyclopropane anesthesia.[22] The anesthetist then has the advantage of having two or three gas anesthetics available plus oxygen plus carbon dioxide and an ether vaporizer, as well as a closed circuit or breathing device with a soda-lime attachment. Of considerable help is the use of exceedingly fine flow meters so that rates as low as 100 cc. or less may be accurately registered.[72] Leech [73] described a special pharyngeal bulb gas-way for use with this system.

Knight and Urner [51] described a special device for self administration of cyclopropane in obstetrical analgesia, which consists of a mask, an inhalation bag, a one-way exhalation valve and a two-gallon supply bag three-fourths full of cyclopropane, a gas regulator and a pressure bulb—all attached by rubber tubing. With this apparatus no gas is given until the bulb is pressed at the onset of pain, when it is rapidly operated and the patient takes deep breaths until relief is obtained. Deep analgesia or early anesthesia supervenes and prevents further operation of the bulb, and hence there is automatic cessation of cyclopropane. The patient recovers rapidly and waits in full consciousness for the next pain. The procedure is generally not instituted until the pains have become severe and the cervix dilated about 4 cm. It is said to aid full contraction, and it is thought that with its use labor progresses more rapidly. It is necessary to have the room well ventilated, and to be certain that there is no pressure on the reservoir, which is never left attached to a tank of cyclopropane.

TYPES OF CASES

Bogan [43] reported on the use of cyclopropane in 300 surgical anesthesias in patients ranging in age from 5 to 84 years. He believed that the high oxygen concentration was especially useful in the young and old. In this series, 145 patients were given cyclopropane, sixty cyclopropane and ether and 100 cyclopropane and avertin with amylene hydrate with either morphine or pentobarbital sodium.

Griffith [65] reported the use of cyclopropane in 1,108 cases of which 592 were abdominal procedures. Tucker [44] employed cyclopropane in 139 major operations, including the case of one 6 year old child given six satisfactory cyclopropane anesthesias in connection with an appendectomy complicated by pleurisy and peritonitis. One of his patients was desperately ill with diabetes and required amputation of the leg, with blood pressure of 240 systolic, 100 diastolic. The anesthesia was satisfactory, but death ensued from a cerebral hemorrhage.

Burford [74] employed cyclopropane in 475 cases and obtained satisfactory anesthesia in "desperate surgical risks" without

72. Romberger,[22] Sanders and Fink.[46]

73. Leech, B. C.: Pharyngeal Bulb Gasway for Cyclopropane Anesthesia, Anesth. & Analg. **16**: 22 (Jan.-Feb.) 1937.

74. Burford, G. E.: Continuous Flow Administration of Cyclopropane, Anesth. & Analg. **15**: 254 (Sept.-Oct.) 1937.

death or accidents. Morgan,[64] Griffith and others analyzed 100 cases of cesarean section under cyclopropane. Bonham[50] reported its use in 732 cases. Griffith used it in patients whose ages ranged from 10 days to 85 years.

OBSTETRICS, THYROID SURGERY AND THORACIC SURGERY

Knight discussed the use of cyclopropane in obstetrics—by filling the bag with a 10 per cent mixture and with each pain instructing the patient to exhale and then take two inhalations of the mixture while bearing down. He believes that the anesthetic does not retard the pains, although it abolishes them and probably hastens delivery. For episiotomy the gas flow is increased to about 10 gallons an hour for three or four inhalations. The same mixture is used for the delivery proper and the Credé expression of the placenta. In many cases relaxation was sufficient to preclude episiotomy and to aid instrumental delivery. He does not believe that oozing is increased and is certain that uterine bleeding is not increased. Morgan believes that there is less blood lost from the uterus in cyclopropane anesthesia and did not encounter any maternal deaths. He compared these results with a series of ethylene-ether anesthesias in which there were two deaths in seven cases of dynamic ileus. Bonham[50] believes that the use of cyclopropane is especially indicated in obstetrics because of the marked contractions of the uterus which occur under cyclopropane anesthesia.

Sise[9] considers cyclopropane useful in meeting the problems of thyroid surgery anesthesia. Goetsch[75] compared cyclopropane with other anesthetics in a series of thyroidectomies in which nitrous oxide was used in thirty-three cases, cyclopropane in fourteen cases, ethylene in eight cases and cyclopropane and procaine hydrochloride in one case. In spite of the fact that the cyclopropane series included complications consisting of one pulmonary embolism with infarction, one typical shock, one moderately severe shock and one fatal thyroid crisis, the author believes that cyclopropane will replace nitrous oxide-ether for thyroidectomy. It is reported that he has stated that he encountered 50 per cent arrhythmias during thyroidectomy with cyclopropane unless nitrous oxide was combined with it.[76] He warned about the danger of hyperventilation and noted that the apnea, which is sometimes seen, may be due to hyperoxidation and suggested the use of carbon dioxide and artificial respiration when apnea occurred.

Eversole and Overholt[77] discuss the difficulties of anesthesia in thoracic procedures. The principal difficulties encountered, of course, arise from the fact that the pathologic condition exists in the organs of the respiratory system, which are also employed for anesthesia. Specifically, the difficulties are: 1. The absorption area is reduced and abnormal amounts of mucus and secretions are formed. 2. There is an increased tendency to cough and the good lung, if any, is in a dependent position and may become contaminated during anesthesia and surgery. Pneumotherapy presents the additional problem of embarrassing both the respiratory and the circulatory system, and it is, therefore, especially important to employ the closed system of anesthesia because of the control of interpulmonary pressure, which is obtainable in no other way. Using an anesthetic mixture of 20 per cent cyclopropane and 80 per cent oxygen these authors found the mixture to be a fairly satisfactory anesthetic agent in these cases. Little absorptive area is necessary; in fact, they believe that one quarter of the area of the normal lung is adequate for maintaining quiet, shallow respirations under cyclopropane anesthesia. Using other agents, they encountered anoxemia, cyanosis, accumulation of carbon dioxide, stimulation of the respiratory movements and rising pulse. Rovenstine[78] also reported the use of cyclopropane in thoracic surgery. He pointed out that because it is not a respiratory stimulant the excursions of the chest are lessened considerably. He did not encounter laryngeal spasm and stated that its advantages include rapid induction, abundant oxygen, abolishment of laryngeal reflexes and ease of endotracheal intubation. It has no disagreeable odor, is nonirritant and hence does not produce mucus. Rovenstine's experience comprises 4,000 clinical cases, but this report refers to 160 cases of thoracic surgery. There was an 8 per cent mortality: one case during operation, one during the first day, five more during the first week and six more than five weeks later. With the exception of the first two cases, which were circulatory in nature, they all presented postoperatively pathologic changes in the lungs, although it is granted that poor anesthetic technic would certainly increase the morbidity in such cases as these.

HOMOLOGUES OF CYCLOPROPANE

Henderson and MacDonald[79] experimented with the methyl cyclopropanes—1:2 dimethyl and 1:2:3 trimethyl—and found them unsuitable for anesthesia, producing more cardiac irregularities than cyclopropane, producing low blood pressure and deleterious effects on cardiac contractility as well as more marked tonus effects.

Lott, Christiansen and Shackell[80] found effective concentrations and lethal concentrations about equal for 1: methyl cyclopropane and cyclopropane but found more undesirable side effects with the methyl compound.

SUMMARY

A brief review and analysis of this material follows:

From the chemical and physical properties it is seen that cyclopropane has the same potential danger of explosibility as the more commonly used ethyl ether. There are several brands available, one of which is made by a different process than the others. There is the possibility that there may be impurities present in the commercial brands. There appears to be an unusual effect on the heart, since arrhythmias have been encountered that are not ordinarily seen with ether anesthesia. Experience has indicated that epinephrine or other sympathomimetic amines should not be administered during anesthesia with cyclopropane. For this reason, as well as because the ordinary signs of anesthesia are not useful, it is necessary to watch the pulse very closely during administration of cyclopropane. The gas has a not unpleasant odor and is not ordinarily considered to be irritant. The question of whether laryngospasm is more frequent with other agents remains to be settled. The incidence of pulmonary complications seems to be no greater than or not as great as the incidence following ether anesthesia. In anesthetic concentrations there does not seem to be a deleterious effect on the liver. The kidney output is similar to that seen with ether and ethylene. Headache may occur more often than with ether anesthetics. The other pharmacologic effects of the drug are discussed. The signs of the various stages of anesthesia are described. It is important to note that it is recommended that no one attempt to administer this gas who is not thoroughly familiar with its properties and with the signs that are available to indicate the depth of anesthesia; these differ from the signs for other anesthetic agents. Many authorities believe it preferable to use the closed technic and, because the respiratory center is not stimulated, premedication that affects the respiratory rate should be used with caution. Details of induction, maintenance and recovery are given, relaxation and oozing are discussed and the use of various types of gas machines are mentioned. There seems to be no special type of case in which cyclopropane should be avoided, with the possible exception of certain cardiac conditions, because of the tendency of the agent to produce arrhythmias. Its usefulness in obstetrics both as an anesthetic and for analgesia and in thyroid and thoracic surgery is described. Brief mention is made of the homologues of cyclopropane.

This review indicates that cyclopropane is a suitable anesthetic agent when used cautiously by those fully informed of its properties, potential dangers and signs which indicate the stages of anesthesia obtained with this agent.

75. Goetsch, Arthur: Cyclopropane Anesthesia in Thyroidectomy, Ann. Surg. **104**: 982 (Dec.) 1936.
76. Livingston, H.: Personal communication to the Council.
77. Eversole, U. H., and Overholt, R. H.: Anesthesia in Thoracic Surgery, J. Thoracic Surg. **5**: 510 (June) 1936.
78. Rovenstine, E. A.: Cyclopropane Anesthesia in Thoracic Surgery, Anesth. & Analg. **14**: 270 (Nov.-Dec.) 1935.
79. Henderson, V. E., and MacDonald, S. F.: Anesthesia with Cyclopropane Derivatives, J. Pharmacol. & Exper. Therap. **61**: 182 (Oct.) 1937.
80. Lott, W. A.; Christiansen, W. G., and Shackell, L. F.: Homologues of Cyclopropane—Methyl Cyclopropane, J. Am. Pharm. A. **27**: 125 (Feb.) 1938.

Council on Foods

ACCEPTED FOODS

THE FOLLOWING PRODUCTS HAVE BEEN ACCEPTED BY THE COUNCIL ON FOODS OF THE AMERICAN MEDICAL ASSOCIATION AND WILL BE LISTED IN THE BOOK OF ACCEPTED FOODS TO BE PUBLISHED.

FRANKLIN C. BING, Secretary.

CLAPP'S STRAINED MIXED GREENS

Manufacturer.—Harold H. Clapp, Inc., Rochester, N. Y.

Description.—Canned strained mixed greens containing equal proportions of kale, lettuce and Swiss chard. Slightly seasoned with salt.

Manufacture.—The fresh kale, lettuce and chard are inspected, sorted, mechanically cleaned and washed. The washed greens are softened by live steam in the absence of air and strained. Salt is added and the strained greens are filled into cans, sealed and heat processed.

Analysis (submitted by manufacturer).—Moisture 93.8%, total solids 6.2%, ash 0.8%, sodium chloride 0.12%, fat (ether extract) 0.4%, protein (N × 6.25) 1.6%, reducing sugars (as invert sugar) 0.3%, sucrose (copper reduction method) 0.2%, crude fiber 0.5%, carbohydrates other than crude fiber (by difference) 2.9%, calcium (Ca) 0.06%, phosphorus (P) 0.04%, iron (Fe) 0.001%.

Calories.—0.22 per gram; 6.2 per ounce.

Vitamins.—No evidence has been provided the Council as to the vitamin content of this product. The method of preparation and processing is designed to retain the natural vitamin values to the highest degree consistent with adequate and safe heating processes. Contact of the product with air during processing is avoided as far as possible.

CELLU BRAND PRUNE PLUM JUICE

Distributor.—Chicago Dietetic Supply House, Inc., Chicago.

Description.—Canned juice expressed from fresh prune plums packed without added sugar.

Manufacture.—Fresh Italian tree-ripened prune plums on which no toxic spray materials have been used are sorted, washed, pitted and preheated. The pulp is pressed through a strong special mesh cloth and the resulting juice is filled into cans, sealed and heat processed.

Analysis (submitted by distributor).—Moisture 85.8%, total solids 14.2%, ash 0.3%, fat (ether extract) 0.5%, protein (N × 6.25) 0.3%, crude fiber 0.1%, carbohydrates other than crude fiber (by difference) 13.0%, invert sugar 6.9%, sucrose 3.7%.

Calories.—0.6 per gram; 17 per ounce.

CALIFORNIA FRESH FLAVOR BRAND KADOTA FIGS FANCY QUALITY

Manufacturer.—Beckwith Packing Corporation, Turlock, Calif.

Description.—Canned Kadota figs, packed in syrup containing a mixture of sucrose and corn sugar, with added lemon juice and salt.

Manufacture.—Ripe Kadota figs are hand sorted, mechanically graded for size, and blanched with steam and light hot water sprays. Cans are filled with fruit and syrup containing a mixture of sucrose and corn sugar, with added lemon juice and salt, preheated, sealed and heat processed. The fruit is sprayed with calcium sulfate, the last application being made not later than fifteen days before the fruit is gathered. According to the information submitted by the manufacturer, the blanching process, which draws the sap from the skin of the fruit, reducing the thickness of the outer portion, is adequate to remove any spray residue which might remain on the fresh fruit.

Analysis (submitted by manufacturer).—Moisture 67.2%, total solids 32.8%, ash 0.5%, fat (ether extract) 0.1%, protein (N × 6.25) 0.5%, total sugars as invert sugar 28.8%, crude fiber 0.6%, carbohydrates other than crude fiber (by difference). 31.0%, acidity (as anhydrous citric acid) 0.1%.

Calories.—1.27 per gram; 36 per ounce.

W. N. CLARK BRAND TOMATO JUICE

Manufacturer.—W. N. Clark Company, Rochester, N. Y..

Description.—Canned tomato juice, seasoned with salt.

Manufacture.—Fully ripe tomatoes are inspected, washed, again inspected, scalded, mechanically sliced, and preheated in an atmosphere of steam. The juice is extracted, seasoned with salt, heated to 85 C. and automatically filled into cans which are sealed and heat processed.

Analysis (submitted by manufacturer).—Moisture 93.1%, total solids 6.9%, ash 1.1%, sodium chloride 0.6%, fat (ether extract) trace, protein (N × 6.25) 1.0%, reducing sugars before inversion, as dextrose 3.2%, reducing sugars after inversion, as dextrose 3.1%, crude fiber 0.2%, carbohydrates other than crude fiber (by difference) 4.2%, titratable acidity as citric acid 0.4%.

Calories.—0.2 per gram; 6 per ounce.

Vitamins.—Chemical titration shows an average of 0.156 mg. of ascorbic acid (3.12 international units of vitamin C) per cubic centimeter; 92 international units of vitamin C per fluidounce.

CRADLE BABY BRAND STRAINED AND SEEDLESS FIG JAM

Manufacturer.—Glaser, Crandell Company, Chicago.

Description.—Canned strained fig jam sweetened with sucrose. The jam may contain small amounts of added acid and/or pectin.

Manufacture.—Dried California figs are washed, softened in sufficient warm water to cover the fruit and sieved. Sugar is added (and pectin and acid if needed to obtain the desired consistency); the batch is mixed and the mixture concentrated under vacuum at 60 C. to not less than 68 per cent soluble solids. Glass jars are automatically filled and are sealed in a high temperature steam vapor chamber.

Analysis (submitted by manufacturer).—Moisture 25.5%, total solids 74.5%, water-insoluble solids 1.5%, water-soluble solids 73.0%, ash 0.6%, protein (N × 6.25) 0.8%, crude fiber 0.3%, carbohydrates other than crude fiber (by difference) 73.0%, acidity 0.2%.

Calories.—2.95 per gram; 84 per ounce.

KAFFEE-HAG DECAFFEINATED COFFEE

Manufacturer.—General Foods Corporation, New York.

Description.—A blend of selected roasted coffee from which almost all the caffeine has been removed.

Manufacture.—Green coffee is cleaned, steamed and the caffeine extracted with trichloroethylene, which is removed by steam distillation. The different coffees are blended in proportions designed to produce a standard beverage, roasted and automatically packed under vacuum in tins. The manufacturer states that each batch is tested to insure at least 97 per cent removal of caffeine.

Analysis (submitted by manufacturer).—Moisture 1.6 %, water-soluble solids 22.1%, ash 4.2%, fat (petroleum ether extract) 16.9%, protein (N × 6.25) 12.1%, caffeine 0.03%, crude fiber 11.5%, tannins 3.3%, carbohydrates other than crude fiber (by difference) 53.7%.

MRS. PALEY'S BABY FOOD—STRAINED BEETS

Manufacturer.—Paley-Sachs Food Company, Houston, Texas.

Description.—Canned, cooked sieved beets slightly seasoned with salt.

Manufacture.—Fresh beets are washed, pressure cooked until just soft enough to sieve, cooled in dilute salt solution, peeled, sieved, filled into glass jars, vacuum sealed and heat processed.

Analysis (submitted by manufacturer).—Moisture 91.6%, total solids 8.4%, ash 0.6%, fat (ether extract) 0.1%, protein (N × 6.25) 1.2%, reducing sugars as dextrose—trace, sucrose 3.7%, crude fiber 0.8%, total carbohydrates other than crude fiber (by difference) 5.7%, calcium (Ca) 0.024%, phosphorus (P) 0.032%, iron (Fe) 0.004%.

Calories.—0.3 per gram; 9 per ounce.

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SATURDAY, MARCH 18, 1939

STERILIZATION OF AIR IN THE OPERATING ROOM

Modern atraumatic aseptic technic in the operating room has almost eliminated infection of wounds in clean cases. However, the introduction of major surgical procedures involving exposure of large raw areas for a long time has again raised the problem of occasional infection. Recently Hart [1] of the Duke University School of Medicine has reported studies during the past five years of efforts to eliminate the occasional sporadic operating room infection. After carefully checking all possible sources of infection, Hart concludes that the least controlled source of infection was air-borne bacteria. Most of the infections were caused by Staphylococcus aureus-haemolyticus. The organisms entered the wound from the air rather than from the skin of the patient. The air was contaminated by the operating room personnel and patients. All supplies and all procedures in the operating room technic were checked by the culture method and were found to be satisfactory except for the air, which was heavily contaminated with Staphylococcus aureus-haemolyticus. The personnel of the operating room and the general population were found at times to have Staphylococcus aureus in the nose and throat in as high as 78 per cent of the cases. A reduction of from 60 to 80 per cent was accomplished by reducing the number of persons in the operating room to the minimum, insistence on masks worn over the nose and mouth at all times, and elimination from the operating room of all persistent carriers of Staphylococcus aureus or of Streptococcus. The rooms were painted frequently and washed daily with an antiseptic solution. By forced ventilation the contaminated air was replaced by clean, washed air taken from above the roof. Despite these measures the number of organisms in the air was not reduced sufficiently to eliminate all infections. In every case of infection in which cultures of the air had been taken the organism cultured from the wound was identical with the one cultured from the air during the operation.

The bacteriologic studies carried on daily convinced the author that the most important source of wound infection was not the bacteria present in the skin but the organisms eliminated from the noses and throats of the operating room personnel. The wearing of thick gauze masks was not apparently an adequate protection against this source of contamination. To eliminate this source the author turned to irradiation of the air. The problem consisted of designing a source of radiant energy which would provide a sufficiently high level of bactericidal radiation to destroy the bacteria without, at the same time, injuring the patient. The Westinghouse Lamp Company, at the request of the author, designed and constructed a special radiant energy apparatus which answers the requirements. An operating room was equipped with eight of these lamps, each 30 inches long. Two blond volunteers from among the students were exposed to radiation from these tubes for eighty minutes and received only a slight reddening of the exposed area, which disappeared within twenty-four hours. The author found that it was possible with eight tubes operating to kill a lightly sprayed culture of Staphylococcus aureus-haemolyticus on blood agar plates within sixty seconds or a heavily sprayed culture within less than five minutes. Practically all organisms exposed to the radiation from these tubes at a distance of 8 feet from the center of the cluster were killed within less than ten minutes, and at a distance of 10 feet within less than thirty minutes. In the corners of the room, 13 feet from the center of the cluster and 11 feet from the nearest tube, the number of viable organisms falling out of the air was reduced from 60 to 90 per cent. The air of the entire room could not be completely sterilized within one hour with only eight tubes and, when they were turned off, recontamination quickly occurred if people were present.

In a series of 132 individual stages of extrapleural thoracoplasties on fifty-nine patients performed in a field of air sterilized by means of bactericidal radiant energy, Hart [2] was able to report a lowering to one half of mortality due to infected wounds. There was an incidence of 3.8 per cent of skin infections as compared with 33 per cent in a previous series of 100 similar operations. The incidence of postoperative elevation of temperature was lowered so that more than two thirds of the patients did not have more than two recorded elevations above 38 C. (100.4 F.) as compared to one third of the patients without radiation who fell in this group. The wound healing has been more rapid and with less reaction when reopened for the second and third stages of thoracoplasty than in those cases in which radiation was not used. In practically all

1. Hart, Deryl: Operation Room Infections: Control of Air-Borne Pathogenic Organisms, with Particular Reference to the Use of Special Bactericidal Radiant Energy, Preliminary Report, Arch. Surg. **34**: 874 (May) 1937.

2. Hart, Deryl: Sterilization of the Air in the Operating Room with Bactericidal Radiation: Comparative Analysis of 132 Individual Stages of Extrapleural Thoracoplasties Performed With Radiation and 110 Stages Performed Without Radiation, J. Thoracic Surg. **7**: 525 (June) 1938.

cases the postoperative pain has been less and convalescence has been more rapid.

In a later report [3] the author presents an analysis of the results obtained in 456 clean primary incisions and eighty-six reopened clean incisions of more than 800 operations performed in the field of bactericidal irradiation. The operations were gastric or intestinal resections, cholecystectomies, mastectomies, appendectomies and amputations of gangrenous extremities. The analysis reveals that postoperative infections have been reduced more than 85 per cent. The occasional death anticipated from infection of a wound did not occur. The number of patients with postoperative temperature above 38 C. has been reduced in thoracoplasties from 68 to 30 per cent, in radical mastectomies from 46 to 34 per cent and in inguinal herniorrhaphies from 36 to 22 per cent. The number of patients with a temperature above 37.5 C. (99.2 F.) for more than four days after operation has been decreased in thoracoplasties from 78 to 22 per cent, in radical mastectomies from 54 to 21 per cent, and in inguinal herniorrhaphies from 46 to 14 per cent. There has also been noted a more rapid wound healing, a lessened systemic reaction and a shortened convalescence.

The bacteriologic studies carried out by Hart and his co-workers, as well as the practical results obtained, seem to establish that air is an important source of contamination in every operative wound. They demonstrated further that sterilization of the air in the operating room can be accomplished by bactericidal irradiation. The method of bactericidal air irradiation may prove to be an important addition to efforts for eliminating infections of wounds in clean primary incisions.

SECONDARY ANTIGENS IN RHEUMATIC FEVER

The demonstration of secondary antigens and antibodies in rheumatic fever recently reported by Coburn and Pauli [1] of Columbia University is clinical confirmation of a speculative hypothesis proposed a decade or more ago by immunologists.[2] If confirmed, this renaissance of the speculative theory of secondary anaphylaxis and immunity may lead to practical diagnostic and therapeutic methods in numerous infectious diseases.

The New York clinicians picture the evolution of rheumatic attacks in three distinct phases. Phase 1 is an acute pharyngeal infection usually of not more than three days' duration, hemolytic streptococci being the causative agent. This is followed by an afebrile, symptom-free period (phase 2) commonly lasting about fourteen days. Phase 3, the period of acute rheumatic symptoms, often shows one or more cycles of activity.

From their point of view the second period (phase 2) is the crucial stage in the genesis of rheumatic symptoms. Only one serologic abnormality has been definitely established during this period, a diminution in serum complement.[3] A still further reduction in complement titer takes place during the acute attack (phase 3). Since decreases in serum complement are known to take place when antigen and antibody coexist in the circulation, Coburn and Pauli postulate the existence of a phase 2, prerheumatic antigen, reacting with a phase 3 antibody as a cause of this complement "deviation."

To test this hypothesis, blood samples were taken at least once a week from rheumatic subjects recovering from hemolytic streptococcus pharyngitis. The resulting serums were preserved with merthiolate, stored at 5 C. and afterward cleared by high speed centrifugation or by Chamberland filtration; 0.1 cc. of the presumptive antibody-containing serum (phase 3) was layered over 0.1 cc. of the presumptive antigen serum (phase 2) and flocculation reactions were recorded after ten minutes at room temperature, after two hours at 37 C. and at the end of twenty-four hours at 5 C. The following scale of precipitin reaction was adopted: "cloudy whirl" (+), "small flakes or granules, supernatant clear" (++) and "large flakes" (+++).

Serums taken by the New York clinicians at the height of the rheumatic attack (phase 3) almost invariably showed definite precipitates (++) with the prerheumatic serums (phase 2) of the same individual. No reactions were noted between phase 1 and phase 2 serums or between phase 1 and phase 3 serums, nor would two phase 2 serums or two phase 3 serums from the same individual react with each other. A mixture of phase 2 and phase 3 serums was necessary to demonstrate the hypothetic antigen-antibody reaction.

Cross reactions of varying intensity were obtained between phase 3 and late phase 2 serums of different patients, the intensity of the reaction varying with the severity of the rheumatic attack. One patient with rapidly fatal fulminating rheumatism, for example, gave +++ reactions with the six heterologous phase 2 serums tested.

The controls included the serums of patients who had recovered from hemolytic streptococcus pharyngitis without subsequent development of rheumatism. Thirty-seven of the forty-seven control tests thus made were negative. As further controls it was shown that normal human serum and serums taken during nonrheumatic fevers were also consistently negative when layered over either phase 2 or phase 3 rheumatic serum.

An attempt was made to determine the nature of the presumptive phase 2 prerheumatic antigen by a study of control reactions with streptococcus antigens isolated from the same patient during the initial pharyngitis. Group specific carbohydrates, nucleoproteins and

3. Hart, Deryl: Sterilization of the Air in the Operating Room by Bactericidal Radiant Energy: Results in Over Eight Hundred Operations, Arch. Surg. **37**: 956 (Dec.) 1938.

1. Coburn, Alvin F., and Pauli, Ruth H.: J. Exper. Med. **69**: 143 (Jan.) 1939.

2. Manwaring, W. H.; Marino, H. D.; McCleave, T. C., and Boone, T. H.: J. Immunol. **13**: 319 (May) 1927.

3. Veil, W. H., and Buchholz, Bruno: Klin. Wchnschr. **11**: 2019 (Dec. 3) 1932. Coburn, A. F.: Lancet **2**: 1025 (Oct. 31) 1936.

"M-substance" were prepared from these autogenous streptococci. Mild precipitin reactions were obtained with one or more of these fractions plus phase 3 serum. These reactions, however, were not parallel with reactions to the patient's own phase 2 serum. Absorption of the phase 3 antibodies with the streptococcus antigens led to a complete removal of the streptococcus precipitins with little or no reduction in anti-phase 2 rheumatic titer. Tests with specific antistreptococcus antibodies of both human and veterinary origin were also negative.

The conclusion seems inevitable that the hypothetic phase 2 prerheumatic antigen is not a streptococcus product or an anti-streptococcus albumin or globulin. This seems to narrow the possibilities to the assumption that the phase 2 prerheumatic antigen is some secondary colloidal product arising from the primary reaction of hemolytic streptococci on pharyngeal tissue. Denatured cartilaginous material, for example, might be conceived as the source of this secondary antigen. A heterophil anticartilaginous antibody, although purely hypothetic, might be the basis for a plausible "inverse anaphylactic" theory of acute rheumatism.

While the possibility was borne in mind by the Columbia investigators that phase 2-phase 3 flocculation may not be due to a specific antigen-antibody reaction, the theory suggested or implied by their data is a stimulating working hypothesis for future serologic and biochemical research. The historical theory of secondary antigens and antibodies is presumably also applicable to numerous other microbic infections. The possibilities of using phase 3 rheumatic serum therapeutically or as a diagnostic agent (cutaneous test) have not yet been tested.

Current Comment

TRICHINOSIS IN THE UNITED STATES

The recent evidence from necropsies that 36 per cent of the inhabitants of Cleveland have trichinosis must not be interpreted as proof that Cleveland is the most highly infested area in the United States. It suggests rather that the routine diagnostic methods employed by earlier investigators were fallacious. Routine examinations of the diaphragms of adult cadavers by the Baermann digestion method led previous investigators to the conclusion that approximately 13.67 per cent of all persons in or around Washington, D. C., are infested with trichinae, 17.5 per cent in Minneapolis and Rochester, N. Y., 24 per cent in San Francisco and 27.6 per cent in Boston. Hall and Collins,[1] however, showed that the routine Baermann technic failed to detect about 29.3 per cent of the positive cases. Evans[2] of the Institute of Pathology, Cleveland, therefore supplemented this routine diagnostic method by application of the newer compression microscope technic. In this technic 1 Gm. samples of the diaphragm, intercostal muscle and sternomastoid muscle are compressed between two pieces of plate glass and examined microscopically. Parallel digestions were made with 100 Gm. samples of the the same muscles. Diaphragmatic digestion alone revealed the presence of twenty cases of trichinosis in 100 consecutive necropsies. This is about the average of the percentages reported by previous investigators. Many cadavers, however, whose diaphragms were negative showed trichinae in one or both of the skeletal muscles. Combining all positive data, Evans found thirty-six positive cases of trichinosis in the first hundred Cleveland necropsies studied by his double technic. Applying the implied correction coefficient (36/20) to the percentages previously reported from other cities, one would conclude that there are presumably the following percentages of trichina infestation in other American cities: Washington, D. C., 24.6 per cent, Minneapolis and Rochester, N. Y., 31.5 per cent, San Francisco 43 per cent and Boston 49.7 per cent, an average of 37 per cent infestation of the urban population of the United States. There is no way, of course, of estimating the resulting social or economic loss; but the estimated 48,000,000 cases of trichinosis in the United States is far from being a national asset.

1. Hall, M. C., and Collins, B. J.: Pub. Health Rep. **52**: 468 (April 16) 1937.
2. Evans, C. H.: J. Infect. Dis. **63**: 337 (Nov.-Dec.) 1938.

TUBERCULOSIS IN DRESSED POULTRY

About 3 per cent of the dressed poultry offered for sale in American markets is infected with tuberculosis. In order to test for the possible presence of tubercle bacilli in dressed poultry, W. H. Feldman[1] of the Mayo Foundation removed spleens aseptically from 125 fowls at the time of evisceration by a local dealer. The fowls thus examined included sixty-six young chickens, thirty mature hens, eighteen domestic ducks, four turkeys, three capons and four wild ducks. Each spleen was emulsified in 5 cc. of sodium chloride solution, and 1 cc. of the resulting emulsion was distributed over the surface of four tubes of egg yolk glycerin agar. The tubes were incubated at 37 C. for ten weeks. Positive growths of acid-fast bacilli were obtained from four spleens. One young chicken, two adult hens and one domestic duck were the sources of these four organs. Subcultures from each of the four cases were inoculated in duplicate into guinea pigs, rabbits and chickens. All guinea pigs were without macroscopically demonstrable lesions when killed from six to eight weeks later. Three of the eight rabbits died within two to eighteen days, presumably from intercurrent infection. The five remaining rabbits died or were killed from one to two months later. At necropsy each of the five showed extensive tuberculous lesions. The eight chickens died or were killed at the end of from six to eight weeks, all showing extensive tuberculosis of the so-called Yersin type. From this evidence the investigator concluded that each of the four positive spleens was the carrier of virulent tubercle bacilli of the avian type. Since virulent tubercle bacilli are thus present in about 3 per cent of apparently normal fowls and since no practical method of postmortem inspection will disclose their presence, Feldman concludes that the rearing of fowls for food markets should be prohibited in environments known to be infected with avian tuberculosis.

1. Feldman, William H.: J. Infect. Dis. **63**: 332 (Nov.-Dec.) 1938.

ORGANIZATION SECTION

CITIZENSHIP AND MEDICAL LICENSURE

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In the formulation of rules by boards of medical registration and in the preparation of proposed legislation and proposed amendments relative to the practice of medicine in the several states, provision has been made and is being made in many of the states for the requirement of citizenship for admission to the practice of medicine. In some states the requirement is made by rule of the medical board, in others the provision is by statute.

It is interesting to note that most states have already required either United States citizenship or first papers as a condition precedent to taking the state board examinations. Only the following states require neither full citizenship nor first papers at the present time: California, Illinois, Massachusetts, New Hampshire, New Mexico, New York, Ohio, Texas, Utah and the District of Columbia. Either by state law or by a ruling of the state boards of registration in medicine, the following states now require full United States citizenship: Alabama, Arkansas, Delaware, Florida, Georgia, Indiana, Kansas, Kentucky, Michigan, Missouri, Montana, Nevada, Nebraska, North Carolina, North Dakota, Oklahoma, South Carolina, South Dakota, West Virginia, Wyoming and, except in the case of Canadians, Arizona, Iowa and Minnesota. States now requiring that first papers for United States citizenship must be taken out are Colorado, Connecticut, Idaho, Louisiana, Maine, Mississippi, New Jersey, Pennsylvania, Rhode Island, Virginia, Washington and Maryland except in the case of Canadians. In addition to these requirements there is a great variety of other restrictions. In some states, such as South Carolina and Wyoming, foreign graduates are not accepted under any circumstances. In some other states there is a requirement of a senior year's work in an approved United States medical school and a one year rotating internship in a United States hospital approved for internship training. Still others require that the candidates pass the National Board examination and apparently there is no uniformity whatever as to these special requirements.

In any discussion of this question, the paramount consideration should and must be the maintenance of the standards of health of the public. The primary reason for the establishment of boards of registration and the basis for enacting laws relative to the practice of medicine has been and must be such maintenance of high standards of public health by regulation of the practice of medicine. Of course doctors individually quite naturally consider the economic aspect of the question. In these times of unemployment and financial difficulty it is somewhat open to question whether the profession of medicine stands to suffer more from the competition of newcomers than do other professions and industry generally. It is probably true that in certain areas the influx of well trained foreign physicians has caused a definite hardship to American doctors in certain communities, particularly in the larger cities. It is not the function and duty of medical boards to promote the economic security of doctors as a class but to promote and maintain high standards of education and practice in the field of medicine. Indirectly, those entitled to economic protection by reason of high standards of efficiency, ability and ideals of public service are actually benefited by able administration in boards of medicine. We must seek to eliminate the unfit. The single question therefore arises as to whether alien nationality becomes a factor of unfitness.

I find that it is the consensus of both physicians generally and students of sociology that the adherence to high ethical standards of medical practice constitutes an important factor in the service of a physician to his community. Included in such high ethical standards are standards of social responsibility, a sincere respect for our governmental endeavors for the promotion of public health, the assumption of responsibility of common social welfare, respect for our fundamental system and operation of government and, I might add, a sincere concern for the maintenance of high standards of morality in relation to those matters which our social order and system of government have decreed to be part of our moral fiber. Obviously, the alien who can meet these tests must be the exception rather than the rule of type to be found. It is therefore fitting and proper that we, as physicians, adopt the premise that citizenship of the United States should be included in the qualifications of the individual in whose hands is placed the responsibility for the moral and spiritual, as well as the physical, well-being of the citizens of any community. Thus I have pointed out the basis for the assumption that it is socially expedient and advisable to require citizenship as a condition precedent to the practice of medicine.

THE QUESTION OF LEGALITY

The next question which confronts us, granted that such requirement is expedient and advisable, is whether such provision by rule of the medical board or by statute in any state is legal, that is whether it would be sustained in courts of last resort if attacked by any individual or group. The precise question of whether citizenship may be required as a condition precedent to the practice of medicine has never been before the United States Supreme Court. Examination of the decisions, however, of the United State Supreme Court and of the supreme courts of the various states relative to kindred questions indicates that arguments may be advanced against the validity of such provisions. However, analysis of these decisions does not indicate that the courts, because of such precedents, would decline to sustain such legislation providing for the citizenship requirement. With the help of the Bureau of Legal Medicine and Legislation of the American Medical Association and able lawyers interested in the problem,

Read before the Thirty-Fifth Annual Congress on Medical Education and Licensure, Chicago, Feb. 14, 1939.

I have made a summary of some of the decisions in relation to the question applied to certain occupations.

The constitution of the United States, article VI, clause 2, provides:

> This Constitution, and the laws of the United States which shall be made in pursuance thereof; and all treaties made, or which shall be made, under the authority of the United States, shall be the supreme law of the land, and the judges in every State shall be bound thereby, any thing in the constitution or laws in any State to the contrary notwithstanding.

Anything in the constitution or laws of any state, therefore, that purports to require citizenship as a condition precedent to the issue of a license to practice medicine or to the practice of dentistry is legally void and without force and effect if contrary to the provisions of the constitution of the United States or of any treaty made by virtue of that constitution.

Under the constitution, the crux of our problem lies in the interpretation the Supreme Court will make of the fourteenth amendment, which reads as follows:

> All persons born or naturalized in the United States, and subject to the jurisdiction thereof, are citizens of the United States and of the State wherein they reside. No State shall make or enforce any law which shall abridge the privileges or immunities of citizens of the United States; nor shall any State deprive any person of life, liberty, or property, without due process of law; [and then as it especially applies to us, the following last clause of the amendment] . . . nor deny to any person within its jurisdiction the equal protection of the laws.

The right of a state to enact laws discriminating against the employment of aliens in private industry came squarely before the United States Supreme Court in *Truax* v. *Raich* decided in 1915. This case arose under an Arizona statute that undertook to require every employer of more than five workers at any one time to employ not less than 80 per cent of qualified electors or native born citizens of the United States. An alien who was in danger of losing his employment because of this statute appealed to the courts for protection. The case having reached the United States Supreme Court, the court said:

> Being lawfully an inhabitant of Arizona, the complainant is entitled under the Fourteenth Amendment to the equal protection of its laws. The description "any person within its jurisdiction," it has been frequently held, includes aliens. "The provisions," said the court, "are universal in their application to all persons within their territorial jurisdiction, without regard to any differences of race, of color, or of nationality; and the equal protection of the laws is a pledge of the protection of equal laws."
>
> It is sought to justify this act in an exercise of the power of the State to make reasonable classifications in legislating to promote the health, safety, morals, and welfare of those within its jurisdiction. But this admitted authority, with the broad range of legislative discretion that it implies, does not go so far as to make it possible for a state to deny to lawful inhabitants, because of their race, or nationality, the ordinary means of earning a livelihood. . . .
>
> The authority to control immigration—to admit or exclude aliens—is vested solely in the Federal Government. The assertion of an authority to deny to aliens the opportunity of earning a livelihood when lawfully admitted to a State would be tantamount to the assertion of the right to deny them entrance and abode, for in ordinary cases they cannot live where they cannot work. . . .

The United States Supreme Court had been called on to pass on a similar question in the Chinese Laundry Cases, covered by the citation *Yick Wo* v. *Hopkins*, decided in 1886, cited in *Truax* v. *Raich*, supra. The Chinese Laundry Cases arose under a San Francisco ordinance relating to the establishment and maintenance of laundries. On its face the ordinance did not discriminate against Chinese, but it was so administered as to operate to that end. In holding the ordinance unconstitutional, the United States Supreme Court said:

> The Fourteenth Amendment to the Constitution is not confined to the protection of citizens. . . .
>
> These provisions are universal in their application, to all persons within the territorial jurisdiction, without regard to any differences of race, of color, or of nationality; and the equal protection of the laws is a pledge of the protection of laws. . . .

The constitutionality of a statute forbidding the licensing of aliens as barbers came before the Supreme Court of Michigan in 1902, in *Templar* v. *Michigan State Board of Examiners of Barbers*. Section 5 of act 212 of the Public Acts of Michigan, 1889, provided for the examination and licensing of barbers, but it provided that no person should receive a license who at the time of his examination was an alien. This section, the Supreme Court of Michigan held, so far as it discriminated on account of citizenship, was repugnant to the fourteenth amendment, as denying equal protection of the law. The court said:

> In the exercise of the police power, the legislature has the undoubted right to require, as a prerequisite to his plying his trade, that he submit to an examination. But had it the right to require citizenship? If it had the right to couple that with other requirements, it would have the same right to make that the only requirement. In other words, it would have the right to exclude alien labor wholly. We think the cases cited demonstrate that it had not this power. . . . To hold that he is not entitled to practice this calling, because not a full citizen of the United States, is to deny him rights which are preserved by the fourteenth amendment.

Not only does the fourteenth amendment of the federal constitution seem to preclude a state from denying to aliens, as such, the right to work in the state, if the alien is physically, morally and qualified by training to work, but our treaties with foreign countries have a material bearing on the situation. Our treaty with Germany, for instance, signed in Washington Dec. 18, 1923, and proclaimed Oct. 14, 1925 (44 Stats. 2132), provides in article 1:

> The nationals of each of the High Contracting Parties shall be permitted to enter, travel and reside in the territories of the other; to exercise liberty of conscience and freedom of worship; to engage in professional, scientific, religious, philanthropic, manufacturing and commercial work of every kind without interference; to carry on every form of commercial activity which is not forbidden by the local law . . . and generally to do anything incidental to or necessary for the enjoyment of any of the foregoing privileges upon the same terms as nationals of the state of residence or as nationals of the nation hereafter to be most favored by it, submitting themselves to all local laws and regulations duly established.

Article VI, clause 2, of the federal constitution declares that the judges in every state shall be bound by all treaties made under authority of the United States, anything in the constitution or laws of any state to the contrary notwithstanding. As to the treaties, it is unlikely that any rights would be asserted, as several of the countries have repudiated their treaties with the United States, and for the further reason that our

nationals have been deprived of the benefit of such treaties in those countries.

As I have already stated, the decisions of the courts holding that citizenship cannot be made a requirement for obtaining a license to pursue certain occupations or to conduct certain businesses do not indicate that the same ruling would be applied in the case of the practice of medicine. Courts have uniformly upheld legislation excluding aliens from the practice of law. While the decisions in some instances were based on the argument that a lawyer is an officer of the court and the court an agency of the state, nevertheless other reasons were given for excluding aliens from the practice of law. Under the general police power of the states where matters of health or morals are involved, such exclusions can be sustained on the premise that the type of occupation or profession is inherently one involving public morals and public health. To illustrate, the Supreme Court of the United States has upheld legislation excluding aliens from a license to sell intoxicating liquors for the reason that such occupation, of necessity, involves public morals.

As I have already pointed out in relation to the question of the social advisability of such legislation, the same reasons, I am told by able lawyers, would be used by the courts in sustaining such provisions, that is, on the ground that the practice of medicine involves a high degree of moral and social responsibility to the community, and respect and adherence to the morals and ethical standards of our people. I am further advised that the cases which I have cited refer to a denial of an alien of his right to work. A license to practice medicine does not confer a right to work. It is not a right but merely a conditional privilege to be granted or withheld by the state purely in consideration of public welfare, public health and morals. Chief Justice Charles Evans Hughes, in a case involving the validity of the Oregon Dental Law, restated this oft repeated rule of law; namely, that the right to practice the healing arts is not in itself a right, but only a conditional privilege to be granted or to be withheld, as the health and welfare of the public may require. In view of the fact that courts have gone far in permitting states under their police power to regulate matters of public health and welfare, it is safe to assume that the decisions I have cited will not be controlling nor held to be analogous to this question.

In passing, I recommend that such provisions for the citizenship requirement be incorporated into the medical statutes of the states rather than left to the rules of the board, as from a standpoint of administrative law a legislative enactment of such a far-reaching requirement would withstand any attack more strongly.

CONCLUSIONS

I would leave the thought that, in view of the importance of the problem, should any such legislative provision be attacked in any state, every cooperation and force of legal ability be provided so that a disastrous precedent will not result by reason of inadequate legal counsel and cooperation.

AMERICAN MEDICAL ASSOCIATION STUDY ON MEDICAL CARE

REPORT FROM THE MEDICAL SOCIETY OF DELAWARE

The study, covering the state of Delaware, which has a population of approximately 250,000, was conducted by the Medical Economics Committee of the Medical Society of Delaware. It was assisted in the distribution and the collection of forms by the state board of health and the Wilmington board of health. The compilation of the data and the preparation of the summary were made under the direction of the secretary of the state medical society. The information obtained is believed to furnish the most pertinent facts regarding the availability or lack of medical care in this area.

The information and data are based on reports from 109 physicians, or 36 per cent of the 303 physicians in active practice. No replies were received from dentists, and only seven pharmacists returned their forms. The hospitals all cooperated in supplying information. There are nine general hospitals, including a contagious disease unit and a mental deficiency unit, one army hospital, one mental hospital, two tuberculosis hospitals, one preventorium and one state welfare home.

The health departments were very cooperative in furnishing information and data, and consequently the conclusions on the need and supply of medical care depends a great deal on their information. The Wilmington board of health furnishes medical services, laboratory diagnosis and sanitary supervision. The state board of health, with a component unit in each county, maintains records and vital statistics, makes laboratory tests and maintains sanitation supervision, maternal and child health supervision, communicable and venereal disease controls, tuberculosis sanatoriums, and dental hygiene and public health nurses. All schools, colleges, nurses and relief agencies also contributed valuable information to the Medical Economics Committee for this study.

The consensus of the physicians who returned the forms is that medical care is available to every one. Of 109 physicians supplying information only ten, or 9 per cent, reported that they knew of cases in which any type of medical care was not easily obtainable. Since the 109 physicians are located in all parts of the state, it can be assumed that their experiences are representative of all the physicians in the state. Therefore approximately only twenty-seven of the total 303 active physicians in the state have observed inadequacies of any type of medical care.

The Medical Economics Committee's report on the specific needs for increased facilities for the distribution of medical care, and recommendations for services that should be expanded in order to make medical care more easily obtainable to certain low income groups, follow:

Delaware is a small, compact and conservative state, with a per capita wealth well ahead of most of the states: its terrain is practically level, the roads are excellent, and medical care can easily be reached. As a matter of fact, among the few instances reported of persons receiving no medical care, there must be a fair sprinkling of those who did not know how to secure such care and still another group who did not wish for care at the hands of the regular medical profession. However, by this statement it is not meant to imply that Delaware is a land of plenty, medically speaking,

because certain facilities definitely need to be expanded and there are certain services which should be enlarged; among these are:

1. Increased facilities for Negro tuberculous patients. A bill is now in the legislature which, if passed, will appropriate $150,000 to provide sixty additional beds for this purpose.

2. An increase in beds available for Negro maternity work is desirable, especially outside Wilmington. No program is at present outlined. Within the past year two hospitals in Wilmington have built new maternity wings, including a fairly adequate number of beds for Negroes.

3. There is a need for more public health nurses and/or visiting nursing service, especially in rural New Castle County. The levy court of this county is being petitioned to provide funds for this purpose, as well as an additional county physician or physicians who perhaps will serve on a part time basis.

4. The hospitals throughout the state need additional beds for general medical and surgical care despite the fact that their occupancy last year was approximately 60 to 65 per cent. This is due to the fact that there are certain peaks of the load, during which time the most urgent cases can be admitted and the less urgent cases are placed on a waiting list.

5. The care of the psychiatric sick is limited to one institution, which serves the whole state and which has been the victim for many years of a vicious degree of overcrowding. Whatever remedy for this condition there may be must come from the legislature, before which appropriation bills will be presented.

6. The mentally deficient are being cared for at a state colony accommodating some 468 patients. However, the lack of housing facilities and a sufficient budget prevents some 200 eligibles from being admitted. The legislature is now conducting a special investigation of this institution and its needs.

7. The care of certain of the aged indigents and chronically ill is centralized in one state welfare home, which replaces the three county poor houses. This is a splendid institution but is already overcrowded, and relief is now being sought from the present legislature.

8. The various clinics operated by the state board of health for venereal diseases, tuberculosis, well baby and maternal welfare are scattered throughout the state at strategic points, and this service will be expanded as, when and if the demand can be demonstrated.

9. Certain clinics, notably the birth control clinic, are being conducted by lay organizations, but the clinics so far established under these auspices are well managed and are staffed by the medical profession.

10. The care of the blind is arranged for by the Delaware Commission for the Blind, which does not operate its own clinic but which has not failed to provide adequate services through the various physicians and hospitals.

11. Care of the crippled has been given by the hospitals and medical profession and has seemed to be fairly adequate. Whatever deficiencies there may be today will be remedied within a year by a new hospital-school to be erected by the Nemours Foundation, which was endowed by the will of the late Mr. Alfred I. du Pont and which will be one of the leading orthopedic institutions in the country.

GENERAL NEEDS

The feeling throughout the profession is that physicians should be paid for services rendered to the indigent and near indigent. This introduces a question the answer for which is not apparent with certainty, but certain plans are in the making to provide for this feature. Wilmington has a group hospital service on the board of which the medical profession is adequately represented and which has been functioning for three years with satisfaction to all concerned. It is proposed to extend this coverage to the counties as well as to the city and to include individual memberships in addition to the employed groups, which now make up the 13,000 members. In addition to this feature there is a surprisingly large general demand for medical expense indemnity insurance, and the Medical Economics Committee of the New Castle County Medical Society is at present working on this problem and will in due time propose to the society a plan for its adoption. It is fairly certain that if and when this plan is adopted in Wilmington it will soon thereafter become statewide in its operation.

Delaware has, in lieu of county commissioners, a levy court of each county, which makes appropriations for the maintenance of hospital beds for the indigent on a per diem basis. These appropriations are inadequate, the deficits being met from private sources. If the medical indemnity insurance plan succeeds, it may be proposed that the levy courts, together with appropriations from the state, buy and keep in force the insurance for indigents and near indigents, which may in the long run prove cheaper than the present system of appropriations if there are an equal number who need this service.

In addition to such medical expense indemnity insurance there should be set up at strategic points throughout the state some central authority whose duty it shall be to weed out the indigent and near indigent from those who are able to pay their sickness expense in full or in part.

CONCLUSION

From these statistical data and summaries it will be appreciated that the needs in Delaware are not as acute as they are in many other communities, but it will also appear that neither the profession nor the public is fully satisfied; to remedy these defects, adequate plans and proposals are already in the making.

FIVE PER CENT OF ALL INCOMES FOR RELIEF

Figures recently published by the Social Security Board show that public relief payments have constituted the following percentages of total national income in each year since 1929:

Year	Per Cent	Year	Per Cent
1929	0.1	1934	4.3
1930	0.1	1935	4.4
1931	0.3	1936	4.8
1932	0.9	1937	3.8
1933	2.7	1938	5.0

The amount of money in each type of income in 1938 was as follows:

Compensation of employees		$39,869,000,000
Entrepreneurial income		12,348,000,000
Dividends and interest		8,186,000,000
Payments to veterans		57,000,000
Relief and social insurance		
Direct relief	$1,005,000,000	
Work relief	2,216,000,000	
Insurance benefits	503,000,000	3,724,000,000
Total		$64,184,000,000

OFFICIAL NOTES

MEETING OF THE COUNCIL ON INDUSTRIAL HEALTH

The third meeting of the Council on Industrial Health took place January 11 at the Association Headquarters. Those attending were Drs. Harvey Bartle, Leroy U. Gardner, Henry H. Kessler, Anthony J. Lanza, Allen D. Lazenby, Earl D. Osborne, C. W. Roberts, Stanley J. Seeger, Clarence D. Selby and Carl M. Peterson. Drs. Seeger and Lazenby were elected chairman and vice chairman respectively for the 1939 term.

Other transactions of interest to the profession were as follows:

1. The Committee on Nomenclature reported that its project to provide the profession with a compendium of terms and acceptable definitions relating to industrial health is more than half completed. The authoritative character of the final published material will be augmented by the use of consultants.

2. The Council has on file information regarding most agencies interested in industrial health. It is planned to attach information of this character in the form of an appendix to the published material on nomenclature.

3. Data regarding available opportunities for instruction of physicians in the fundamentals of industrial hygiene were presented. Inadequate provision of undergraduate, graduate and postgraduate training resulted in the formation of a subcommittee to determine the most effective contribution the Council could make for improvement.

4. Additional plans were made for the issuance of useful and authoritative articles to impress on the general profession its opportunities and responsibilities in the industrial health movement. A series of articles is contemplated on medical organization in industry.

5. The Council decided to continue the Congress on Industrial Health as an annual function.

6. At the request of the Council, committees on industrial health and related subjects have been formed in a number of the state medical associations. The importance of these groups and the necessity for regular interchange of information was recognized. A subcommittee was formed to undertake this assignment.

7. The Council decided to continue the development of a clearing house of information as a necessary and desirable service to the medical profession.

8. The best means for analysis and review of medical progress, standards and interest under workmen's compensation procedure were discussed, especially cooperative action with official agencies in the constituent and component societies. In this connection the Council undertook to explore the possibilities for a more scientific approach to the relationships existing between trauma and disease to determine if therein lie better prospects for extraprofessional understanding and acceptance of medical opinion regarding etiology.

9. Conversations with representatives of rehabilitation and compensation groups were deferred until the Council had a better opportunity to discover the exact nature of the problems under discussion and the degree of medical interest involved.

10. The relations of the Council on Industrial Health with the sections of the Scientific Assembly, more particularly the Section on Preventive and Industrial Medicine and Public Health, were considered.

11. The Council agreed that its activities would be facilitated by holding two meetings annually, one in conjunction with the Annual Congress early in the year, and another at midyear subject to adopted regulations.

12. The tenure of office of members of the Council was determined and nominations were considered to fill one vacancy in the present membership.

RADIO BROADCASTS

The radio broadcasts by the American Medical Association and the National Broadcasting Company, under the title Your Health, continue as previously announced each Wednesday over the Blue network of the National Broadcasting Company at 2 p. m. eastern standard time (1 p. m. central standard time, 12 noon mountain time, 11 a. m. Pacific time).

Changes in this time will be necessary to take into consideration daylight saving time. Announcement of this change will appear in advance in THE JOURNAL. Owing to network conflicts the Chicago broadcast will not occur at 1 p. m. on Wednesday but there will be a rebroadcast from a recording over Station WENR at 8 o'clock each Monday evening. The program broadcast each Monday will be identical with the network program of the preceding Wednesday.

It has been necessary to curtail the length of the series by omitting the last two programs, which would have been broadcast June 14 and June 21. The series, therefore, will end with the broadcast scheduled for June 7.

The next three programs to be broadcast, together with their dates and their topics, are as follows:

March 22. Auditing the Health Record.
March 29. Animal Diseases Transmitted to Man.
April 5. Don't Believe Everything!

MEDICAL LEGISLATION

MEDICAL BILLS IN CONGRESS

Changes in Status.—S. 1706 has been reported to the Senate, proposing to provide for reorganizing agencies of the government. H. R. 1776 has passed the House, providing for the assignment of medical officers of the Public Health Service for duty on vessels of the Coast and Geodetic Survey. H. R. 3537 has passed the House, extending facilities of the Public Health Service to officers of the foreign service of the United States.

Bills Introduced.—S. 758, introduced by Senator Wheeler, Montana, and H. R. 3694, introduced by Representative Dempsey, New Mexico, propose to amend the Federal Emergency Relief Act of 1933 for continuation of the civil works program by eliminating the requirement that an injury sustained by an employee must be of traumatic origin to entitle the employee to compensation, including medical and hospital benefits. H. R. 4740, introduced by Representative Boren, Oklahoma, proposes to extend the services of the National Bureau of Standards by providing for establishing performance standards when in the public interest. H. R. 4779, introduced by Representative Tenerowicz, Michigan, proposes to amend the federal income tax law so as to authorize the deduction of amounts paid during the year as fees to physicians and dentists, and the amount expended, not in excess of $500, for funeral expenses. H. R. 4791, introduced by Representative Pfeifer, New York, proposes to establish a federal Department of Health to be headed by a Secretary of Health appointed by the President from the medical profession. This bill is pending in the House Committee on Expenditures in the Executive Departments, of which Representative John J. Cochran of Missouri is chairman.

STATE MEDICAL LEGISLATION

Arizona

Bill Passed.—H. 129 has passed the house and senate, proposing to make it a felony to practice or attempt to practice medicine without having a valid recorded license so to practice issued by the State Board of Medical Examiners. The present law makes it a felony to practice or attempt to practice without having a valid recorded certificate.

Bill Introduced.—H. 276 proposes that a person shall not be entitled to hospitalization or medical care at public expense unless he or she has continuously resided in the state for at least three years immediately preceding the date of application for relief.

California

Bills Introduced.—A. 1727 proposes to require hospitals to keep hospital records on file for at least three years after the persons to whom the records apply are discharged and to permit patients and ex-patients or persons they designate to examine, inspect or copy the pertinent records. S. 492 proposes to direct the Director of Institutions, with the approval of the State Board of Control, to provide suitable property for one or more institutional units to be known as State Inebriate Colonies and to be used for the isolation and rehabilitation of chronic inebriates committed thereto by appropriate courts. A. 2748 proposes to give the juvenile court jurisdiction over any person under 21 years of age who is afflicted with syphilis, gonorrhea or chancroid and who is in need of medical and custodial care, or both.

Connecticut

Bill Introduced.—S. 305 proposes to establish a department of professional and vocational licensing, to be in charge of an executive secretary, who is to be a secretary of each of the licensing boards and commissions of the state, including the state board of healing arts, the medical examining board, the homeopathic medical examining board, the osteopathic board, the chiropractic board, the naturopathic board, the optometry board, the chiropody board, the dental commission and others. The executive secretary is to exercise all the powers and perform all the duties conferred or imposed on the secretary of the boards enumerated.

Colorado

Bills Introduced.—H. 466 proposes as a condition precedent to the issuance of a license to marry that each party to a prospective marriage present a physician's certificate that he or she has submitted to such examination, including a standard serologic test, as may be necessary for the discovery of syphilis and that in the opinion of the physician the party either is not infected with syphilis or is not in a stage of that disease which may become communicable. H. 470 proposes to require every physician attending a pregnant woman to take or cause to be taken a sample of her blood within ten days of the first professional visit and to submit that sample to an approved laboratory for a standard serologic test for syphilis.

Delaware

Bills Introduced.—S. 79 proposes to enact a law regulating the manufacture, sale, distribution or advertising of foods, drugs, cosmetics and devices. H. 141 proposes to repeal the existing laws providing compensation for workers injured or acquiring stated occupational diseases in their employment and to enact a new workmen's compensation act. The bill proposes to provide compensation to workers (1) suffering personal injury arising out of and in the course of their employment, (2) contracting disease or infection as naturally results directly from the industrial injuries or (3) contracting from their employment the following occupational diseases: anthrax, lead poisoning, arsenic poisoning, phosphorus poisoning, poisoning from benzene and its homologues, wood alcohol poisoning, chrome poisoning, caisson disease, radium poison, or poisoning from carbon disulfide or hydrogen sulfide. The bill proposes to require the employer during the first thirty days after the injury to furnish reasonable surgical, medical and hospital services, medicines and supplies, not to exceed in cost, however, $150. The workmen's compensation bureau, which is to administer the act, may in its discretion require the employer to furnish additional surgical, medical and hospital services, medicines and supplies as and when needed, for such further period as it shall deem necessary. H. 76 proposes to direct the State Board of Trustees of the Delaware State Hospital at Farnhurst to establish a psychiatric observation clinic for the observation, study, psychiatric diagnosis and treatment of persons suffering from mental and nervous diseases. H. 143 proposes to prohibit the retail sale and distribution, except on the written prescription of a licensed physician, dentist or veterinarian, of barbital, sulfonethyl methane (trional), sulfonmethane (sulfonal), diethylsulfone, diethylmethane (tetronal), paraldehyde, chloral or chloral hydrates, chlorobutanol.

Georgia

Bill Passed.—S. 117, to amend the chiropractic practice act, passed the senate February 22, proposing (1) to require applicants for licenses to practice chiropractic to have graduated from chiropractic schools which require for graduation a period of active attendance equivalent to a standard four year college course, instead of the present requirement that such applicants have graduated from chiropractic schools requiring a course of three years of six months each and (2) to require chiropractic licentiates to renew their licenses annually and to condition that renewal on attendance during the preceding year at least one of the two "educational" programs conducted by the Georgia Chiropractic Association.

Illinois

Bills Introduced.—H. 324 proposes to appropriate $25,400 for a cancer diagnostic service by the Department of Public Health. H. 327 proposes to enact a separate naprapathic practice act and to establish an examining committee to examine and license persons to practice naprapathy. The bill attempts to define naprapathy as follows: "Any one or any combination of the following practices, without the use of drugs, serums or operative surgery, constitutes the practice of Naprapathy: (*a*) examination of the human body, to ascertain the presence of defects or abnormal conditions involving the connective tissues; (*b*) diagnosis of aforesaid defects or abnormal conditions; (*c*) prescription, recommendation or advice regarding treatment of aforesaid defects or abnormal conditions; (*d*) treatment of aforesaid defects or abnormal conditions; (*e*) attempting any of the foregoing practices."

Indiana

Bills Enacted.—The following bills have become laws: H. 21 to require every physician attending a pregnant woman to take or cause to be taken a sample of her blood at the time of diagnosis and to submit such sample to an approved laboratory for a standard serologic test for syphilis; H. 37, appropriating $75,000 annually for the fiscal biennium beginning July 1, 1939, for the purchase and distribution free of charge to poor persons of pneumococcus serum, diphtheria toxoid, smallpox virus and typhoid bacterins; H. 134 requiring both parties to a prospective marriage to present a physician's certificate as to freedom from syphilis; and S. 173, to regulate the manufacture, distribution and advertising of foods, drugs, cosmetics and devices.

Iowa

Bills Introduced.—H. 431, to amend the chiropractic practice act, proposes (1) to provide that "The practice of chiropractic shall be deemed to be the adjustment by hand of articulations of the spine and other incidental adjustments, and shall include the right to use air, light, heat, water, diet, and exercise, in the treatment of diseases," and (2) to prohibit a chiropractor "from practicing operative surgery, electro-coagulation, radium in any form, general hyperpyrexia, osteopathy, optometry, obstetrics, x ray treatment, or administering or prescribing any drug or medicine included in materia medica," and (3) to provide that every licensed chiropractor shall place on all signs used by him and to display prominently in his office the word "chiropractor" or "chiropractic physician." H. 180 proposes to appropriate $2,000,000 for the erection of a hospital for the treatment and care of the insane, to care for at least 1,500 patients. H. 543 proposes to make it a ground for the revocation of a license to practice medicine, osteopathy, chiropractic, dentistry, optometry or podiatry for the licentiate to be "guilty of aiding or abetting an unlicensed person to practice, either by direct employment or indirectly through subterfuge or arrangement, whereby the unlicensed person through the use of such professional services profits monetarily in any manner."

Bill Passed.—H. 59 has passed the house, proposing to condition the issuance of a license to marry on the presentation by both parties to the proposed marriage of certificates from licensed physicians that they are either free from syphilis or not in a stage whereby it may become communicable, as nearly as can be determined by a thorough physical examination and such standard microscopic and serologic tests as are necessary for the discovery of syphilis. The bill proposes to limit the fee a physician may charge for such physical examination and standard microscopic and serologic tests to $2 for each person so tested and examined.

Kansas

Bills Introduced.—S. 328 proposes to prohibit a pupil or teacher from attending or teaching in any school, public or private, unless possessing a physician's certificate that he or she has been successfully vaccinated against smallpox or that he or she is not a fit subject for vaccination. H. 348 proposes to direct the State Board of Education to require a course of study in the public schools concerning the evil effects of the use of marihuana, alcohol, narcotics and hypnotic drugs. H. 448 proposes to establish a board of examiners for consulting psychologists to examine and license applicants for licenses to practice as consulting psychologists. The bill proposes to make it unlawful for any one but licentiates to represent themselves as or to assume to act as consulting psychologists. Applicants for such a license must hold a degree of doctor of philosophy in psychology or in education from a college or university recognized by the board of examiners. H. 509 proposes to grant to a hospital furnishing any service to a person injured by an accident not covered by the workmen's compensation act a lien on all rights of action, claims, judgments, settlements or compromises accruing to the injured person because of his injuries.

Maine

Bills Introduced.—S. 414 proposes that in criminal cases in which the defendant is charged with operating a motor vehicle while under the influence of intoxicating liquor the results of scientific analysis of body fluids legally obtained from the defendant shall be admissible as evidence. S. 416 proposes to repeal the existing laws regulating the possession or distribution of narcotic drugs and to enact what appears to be the uniform narcotic drug act.

Maryland

Bill Introduced.—H. 392 proposes to authorize the State Board of Health to establish such minimum standards as it considers necessary for laboratories in the state, except in Baltimore City, which make examinations in connection with the diagnosis and control of human diseases.

Michigan

Bills Introduced.—S. 140 proposes to repeal existing laws relating to coroners and to create a medical examiner system in the state under the direction of a state medical examiner appointed by the governor. The board of supervisors of each county is, with the approval of the state medical examiner, to appoint a licensed physician to serve as a county medical examiner. A county medical examiner is to have jurisdiction only in cases in which a person is supposed to have come to his or her death by violence, without medical attendance or as a result of an abortion or in case a prisoner dies in any city jail. H. 215 proposes to authorize the organization of corporations to establish, maintain and operate nonprofit medical care plans, whereby medical care is provided at the expense of the corporations to such persons or groups of persons of low income as become subscribers to such plans under contracts which entitle each such subscriber to definite medical and surgical care, appliances and supplies, by licensed physicians in their offices, in hospitals and in the home. The bill states that medical care is not to be construed to apply to hospital service. H. 277 proposes to require every physician attending a pregnant woman to take or cause to be taken a sample of her blood at the time of first examination and to submit that sample to an approved laboratory for a standard serologic test for syphilis.

Minnesota

Bills Introduced.—S. 781 and H. 853 propose to prohibit, except on the written prescription of a licensed physician, dentist or veterinarian, the retail sale or distribution of barbital, veronal, proponal, ipral, dial, neonal, sandoptal, amytal, phenobarbital, phanodorn, noctal, allonal, medinal or any preparation, mixture or other substance containing any of the aforementioned substances. S. 683 proposes that any graduate of a chiropractic school who (1) made application for a certificate of registration in the basic sciences before Oct. 1, 1927, (2) is an honorably discharged soldier of the World War and (3) was a resident of the state prior to and since May 1, 1925, shall be entitled to receive a certificate of registration in the basic sciences without examination if he makes application within thirty days after this bill becomes a law.

Missouri

Bills Introduced.—S. 132 proposes to create in the State Board of Health a division of child hygiene to issue educational literature on the care of the baby and the hygiene of the child, to study the causes of infant mortality and the application of preventive measures for the prevention and suppression of the diseases of childhood, to supervise and regulate the physical inspection of public school children and to inspect sanitary and hygienic conditions on public school property. H. 152 proposes that hereafter in the administration of any public health project in the state all doctors of medicine and all doctors of osteopathy must be given equal rights and privileges. H. 500 proposes to require every person licensed to practice medicine in the state annually on or before December 31 to register with the State Board of Health and to pay an annual fee of $1. H. 462, to amend the medical practice act, proposes to require an applicant for a license to practice medicine, in addition to educational qualifications now required by law, to furnish evidence of "completion of premedical education consisting of a minimum of sixty semester hours of college credit in acceptable subjects from a reputable college or university approved by the board of health." H. 548 proposes to permit any person to file an information in the nature of a quo warranto or an action to enjoin or oust from the unlawful practice of medicine any person who practices medicine or surgery without being licensed to do so.

Nevada

Bills Introduced.—S. 8 proposes to establish a state sanatorium for the treatment and care of persons suffering from tuberculosis, to be subject to the control and jurisdiction of the State Department of Health. A. 178 proposes to authorize the sexual sterilization of insane, feebleminded or epileptic inmates of state institutions. The bill further proposes that all prisoners who have previously been convicted of two or more felonies are to be subject to observation and examination by any mental hygiene clinic and, if it is found that the criminality is caused by mental abnormality or mental disease, the prisoner may be sterilized. A. 165 proposes to prohibit a county clerk from issuing a marriage license unless the applicant files "a certificate of the examining physician, duly signed and dated within fifteen days prior to the application, that physical examination and serologic tests do not disclose syphilis in the applicant, that the applicant has submitted to a Wassermann or Kahn or other similar standard laboratory blood test, and that in the opinion of such physician at the time of the examination the applicant either is not infected with syphilis or is not in a stage of that disease which may become communicable."

Bill Passed.—A. 149 passed the assembly March 2, proposing to enact a law regulating the sale, distribution and advertising of foods, drugs, cosmetics and devices.

New Hampshire

Bill Passed.—H. 232 has passed the house and senate proposing to authorize the formation of nonprofit hospital service corporations to maintain and operate plans whereby hospital care may be provided at the expense of the said corporations by hospitals to subscribers to said plans under contracts entitling the subscribers to stated hospital services.

New Jersey

Bills Introduced.—S. 144 proposes to authorize the board of education of any school district to require immunization to diphtheria as a prerequisite to school attendance. A. 210 proposes extensive amendments to the existing medical practice act. Most important, the bill proposes that after 1945 applicants for licenses to practice chiropractic must meet the same educational requirements as are imposed on applicants for licenses to practice medicine and surgery. Such applicants apparently after that date would be given licenses to practice medicine and surgery without restriction. The bill also proposes to limit licensure to citizens of the United States and to authorize a court of chancery to enjoin the unlicensed practice of medicine. A. 245 proposes so to amend the state pure food and drug act as (1) to include also cosmetics and therapeutic

devices and (2) apparently to make it conform generally to the Federal Food, Drug and Cosmetic Act. S. 171 proposes to require every physician, pharmacist and head of every hospital, when any person infected with syphilis, gonorrhea or chancroid applies for treatment, to report the facts to the State Department of Health. The bill further proposes to require any person infected with venereal disease to consult at once a licensed physician or hospital "or any person who practices healing by spiritual, religious or mental means." S. 167, to amend the medical practice act, proposes to limit licensure in the healing arts to citizens of the United States. The present law permits the licensing of persons who have declared their intention of becoming citizens.

New Mexico

Bill Passed.—H. 282 passed the house February 28 proposing to require every practitioner of the healing art attending a pregnant woman to take or cause to be taken a sample of her blood at the time of first examination and to submit that sample to a laboratory approved by the State Department of Public Health or to the State Department of Public Health for a standard serologic test for syphilis.

New York

Bills Introduced.—S. 965, to supplement the medical practice act, proposes to enact a series of provisions with respect to the practice of physiotherapy, which the bill states "means the use for the treatment of diseases, pain, injury, deformity, or physical condition, by means of actinotherapy, hydrotherapy, mechanotherapy, thermotherapy and electrotherapy, exclusive of x-rays." The bill proposes to require a licensed physiotherapist to register annually with the secretary of the board of medical examiners. The bill seems to lack any provision whereby persons other than those now licensed to practice physiotherapy may obtain such licenses. S. 969 proposes to prohibit the practice of radiology except by licensed physicians, osteopaths, dentists or chiropodists, subject, however, to the conditions and limitations of their respective licenses. A. 1308 proposes that no person who has a communicable or contagious disease shall work or be permitted to work in a factory in which a food product is manufactured. The bill also proposes to require any such employee, when required by a medical inspector of the labor department, to submit to a physical examination. A. 1416 proposes to reimburse annually to a city maintaining a hospital for the care and treatment of persons afflicted with tuberculosis one half of the amount appropriated during the preceding year by the city for the maintenance of the hospital. A. 1417 proposes to authorize any city common council to convey to the state any hospital owned and operated by the city for the care and treatment of tuberculosis. Any hospital when so acquired by the state is to be deemed a state tuberculosis hospital and is to be under the jurisdiction and control of the State Department of Health. The cost of its operation and maintenance shall be provided by state appropriations. A. 1428 proposes that a license to practice osteopathy shall entitle the holder thereof to use instruments for minor surgical procedures and to use anesthetics, antiseptics, narcotics and biologic products. The present law specifically states that a license to practice osteopathy shall not permit the holder thereof to administer drugs or perform surgery with the use of instruments. A. 1433 proposes to prohibit, except on the written prescription of a licensed physician, dentist or veterinarian, the retail sale or distribution of barbital, sulfonethylmethane (trional), diethylsulphor diethylmethane [sic] (tetronal), carbromal, chloral or choral hydrate or chlorobutanol. A. 1280 proposes to establish in the motor vehicle bureau a board of motor vehicle accident compensation to assure the payment of medical and hospital expenses resulting from motor vehicle accidents. The bill proposes to require every owner of a motor vehicle either to furnish bond or an insurance policy or to pay $5 in addition to the registration fee now required by law. Any person injured in a motor vehicle accident, if the car involved in the accident is uninsured, may recover from the fund so created expenses incurred for medical, surgical, nursing and hospital services up to $600 to be ratably distributed among those injured. A. 1238 and S. 914 propose to include employment in hospitals within the workmen's compensation act. A. 1265 proposes to prohibit the performance of an operation, the purpose or effect of which is to change or alter the skin or tissues of the fingers or thumbs so as to alter finger patterns or fingerprints. The bill also prohibits the performing of any operation of plastic surgery on a known criminal the purpose or effect of which is to alter his personal appearance and make identification and apprehension difficult. A physician, the bill proposes, must report immediately by telephone, if possible, to appropriate police authorities all requests for operations which seem to come within the prohibitions of this bill. A. 1213 proposes to enact what the bill cites as the New York uniform food, drug and cosmetic act to regulate the manufacture, distribution or advertising of foods, drugs, cosmetics and devices. A. 1585 proposes to prohibit private hospitals from requiring or permitting any employee to work more than eight hours in any day nor more than forty-eight hours in any calendar week.

North Carolina

Bills Introduced.—S. 185 proposes to collect from each applicant for an automobile license 50 cents in addition to existing license fees, to establish the North Carolina Highway Accident Hospitalization Fund, which when it totals $100,000 is to pay $3 a day for up to twenty-one days of hospitalization for every resident of the state sustaining a motor vehicle injury and needing hospital care for his injuries. Any indigent who has suffered a motor vehicle injury is to be entitled to full hospital service for up to twenty-one days and to have the fund pay the entire cost. Persons who are not indigents are to be permitted to apply the amount payable from the fund as a credit on their hospital bill. S. 232 proposes to enact what it cites as the North Carolina food, drug and cosmetic act to regulate the manufacture, distribution and advertising of foods, drugs, cosmetics and therapeutic devices.

Ohio

Bills Introduced.—H. 204, to amend the law prohibiting a physician from testifying concerning a communication made to him by his patient in that relation except by the express consent of the patient, proposes that if the patient is dead the physician may testify by the express consent of the surviving spouse, personal representative or heir of the patient. H. 379 proposes, as a condition precedent to the issuance of a license to marry, that each party to the proposed marriage present a certificate of a physician that he or she is free from epilepsy, feeblemindedness and insanity and is not infected with syphilis, or is not in a stage of that disease which may become communicable, as nearly as these facts can be determined by examination of the party and by the application of standard laboratory tests for syphilis.

Oklahoma

Bill Introduced.—H. 354 proposes to prohibit a licensed practitioner of the healing art, in making professional calls away from his office, from charging or collecting more than his regular fee for each call plus 50 cents per mile for each mile actually and necessarily traveled in going from his office to the place where he attended the patient.

Oregon

Bills Introduced.—S. 426 proposes to prohibit the operation of a maternity hospital or other place for the reception, care and treatment of women during pregnancy or within ten days after delivery, unless licensed by the State Board of Health. S. 435 is apparently a proposal to permit chiropractors, osteopaths and naturopaths to practice "massiotherapy," which is defined by the bill to include all terms defined in section 1 of the bill. Section 1 reads as follows: "For the purposes of this act the following terms shall be construed respectively to include and mean: 1. The word 'massiotherapy' shall mean massage. 2. The word 'hydrotherapy' shall mean the use of water for treating elimination through the pores of the skin. 3. The word 'physiotherapy' shall mean light therapy galvanism, faradism high frequency, diathermy, sinusoidal currents, short wave and any or all other phases of physiotherapy. 4. The word 'electrotherapy' shall mean the therapeutic use of electricity. 5. The words 'physical therapy' shall

mean the use of natural forces such as light, heat, air, water and exercise [sic], a thorough knowledge of physiological and pathological effects on anatomy of the above modalities in the treatment of disease." The bill further provides that all masseuses or masseurs or other technicians having establishments and giving treatments as defined in this act and who have been engaged in practice in the state for six years or more, and who in the opinion of the State Board of Chiropractors or Naturopaths are competent, shall be licensed (by whom the bill does not state) to practice massiotherapy as defined in the bill. S. 475, to amend and supplement the laws relating to the practice of osteopathy, proposes (1) to deprive the board of medical examiners of its present jurisdiction in examining and licensing persons to practice osteopathy and (2) to establish an independent board of osteopathic examiners to examine and to license persons to practice osteopathy. The bill states that "'Osteopath' or 'osteopathic physician' or 'osteopathic physician and surgeon' shall mean one who practices osteopathy and the science of healing as taught in the branches and embraced in the subjects covered by the examination provided for" by the act. The act requires applicants to be examined in anatomy, physiology, chemistry, surgery, bacteriology, histology, pathology, gynecology, obstetrics, theory and practice of osteopathy, diagnosis and hygiene and public health.

Pennsylvania

Bills Introduced.—S. 129 proposes, as a condition precedent to the issuance of a license to marry, that each party to a proposed marriage present a physician's certificate that the party has submitted to an examination and is free from communicable tuberculosis, is not infected with communicable gonorrhea, and is not infected with communicable syphilis as determined by a standard laboratory blood test made not more than ten days preceding the application for license. H. 367 proposes that, whenever in any civil or criminal proceeding issues arise on which the court deems expert evidence is desirable, the court may appoint one or more experts, not exceeding three, on each issue to testify at the trial.

South Carolina

Bill Passed.—H. 361 passed the house February 24 proposing to require every physician, midwife, nurse or other person attending at the birth of a child to instil, or have instilled, in the eyes of the baby, within one hour after birth, a 1 per cent solution of silver nitrate, or some equally effective prophylactic, approved by the State Department of Public Health, for the prevention of blindness from ophthalmia neonatorum. A record of such administration or instillation must be reported on the birth certificate, showing the time with respect to the birth and the kind of prophylactic administered.

Bill Introduced.—S. 325 proposes, in effect, to grant to a physician, dentist, trained nurse, or hospital furnishing care or treatment to an injured person a lien on all judgments and settlements accruing to the injured person because of his injuries.

Tennessee

Bills Introduced.—H. 997 proposes to authorize the organization of corporations to operate nonprofit hospital service plans whereby hospital service may be provided by one or more hospitals which have contracted with such corporations to persons who become subscribers to such plans. H. 821 and S. 584 propose to establish a division of tuberculosis control in the Department of Public Health, which is to provide financial aid to counties or municipalities in the maintenance of patients in tuberculosis hospitals or in wards or pavilions in approved hospitals other than tuberculosis hospitals for the treatment and care of indigent persons sick with tuberculosis. H. 1038 proposes to require a food handler to undergo a physical examination and blood test every six months to ascertain whether or not he or she has tuberculosis or venereal disease and to make it unlawful to employ any such person unless he or she presents a physician's certificate as to absence of tuberculosis or venereal disease. H. 1054 proposes to require all public school teachers to undergo annually a physical examination and to submit to blood tests to determine the presence or nonpresence of tuberculosis and venereal disease. H. 1039 proposes to require physicians attending pregnant women to make the necessary blood tests of the patient to determine the presence of syphilis prior to the birth of the issue. S. 868 and H. 1174, to amend the workmen's compensation act, propose to require an employer to provide an injured workman such medical, surgical and hospital services as are reasonably required to cure or relieve from the effects of the industrial injury. The present law limits such liability to $200 and requires the aid to be rendered only during the first thirty days after knowledge of injury. S. 1003 and H. 1385, to amend the workmen's compensation act, proposes to require an employer, during sixty days after notice of an industrial accident, to furnish free of charge to the injured workman such medical and surgical treatment, medicine, medical and surgical supplies, crutches and apparatus as may be reasonably required, provided, however, that the total liability of the employer for medical and surgical services shall not exceed $100 and for hospital services shall not exceed $300.

Texas

Bill Introduced.—H. 818 proposes to prohibit the admission of a child to school "for the first year of its school life" until he or she has been successfully vaccinated for the prevention of smallpox, typhoid and diphtheria. The bill proposes to make it the duty of the county health officers and city health officers of the state to administer such vaccine as is necessary free of charge.

Vermont

Bills Introduced.—H. 285 proposes to establish within the Department of Public Welfare a psychiatric clinical division to provide local and traveling clinics at such places and at such times as will efficiently examine (1) children under the supervision and jurisdiction of the public welfare department; (2) dependent, neglected or delinquent children against whom court proceedings have been instituted; and (3) children against whom complaints or petitions have been made to the state probation officer. H. 319 proposes, as a condition precedent to the issuance of a license to marry, that each party to the proposed marriage present a physician's certificate that he or she has been given such examination as may be necessary for the discovery of syphilis, including a standard serologic test, made not more than thirty days prior to the date of application for a marriage license, and that in the opinion of the physician the party either is not infected with syphilis or if so infected is not in a stage of that disease which is or may become communicable to the marital partner.

Washington

Bill Enacted.—S. 114 has been enacted as Laws, 1939, C. 46, proposing to establish at Soap Lake an institution to be known as the McKay memorial research hospital for the treatment and care of persons afflicted with Buerger's disease and for study of the disease and of the properties of the waters of Soap Lake.

Bills Introduced.—S. 187, to amend the law establishing in the department of social security a division for improving the condition of the blind and for preventing blindness and providing certain monthly payments to needy blind persons, proposes that medical care or other corrective treatments, such as glasses, earphones and all other appliances, shall be provided by the state to such recipients, and the cost thereof shall not be deducted from blind assistance allotments. S. 374 proposes to require a physician attending a pregnant woman to take or cause to be taken a sample of her blood at the time of first examination and to submit that sample to an approved laboratory for a standard serologic test for syphilis. S. 373 proposes, as a condition precedent to the issuance of a license to marry, that both parties to the proposed marriage present physicians' certificates that they have been given such examination, including a standard serologic test, as may be necessary for the discovery of syphilis and that, in the opinion of the physicians, the applicants are not infected with syphilis or, if so infected, are not in a stage of that disease which is or may become communicable to the marital partner.

West Virginia

Bill Passed.—S. 159 passed the senate February 22 proposing to make it unlawful for any person to use the prefix "Doctor" or "Dr." in connection with his name in any letter, business

card, advertisement, sign or public display of any nature, without affixing thereto suitable words or letters designating the degree which he holds.

Wisconsin

Bills Introduced.—S. 183 proposes (1) to supplement the chapter of the statutes entitled "Construction of Statutes" by proposing definitions of (*a*) "physician," "surgeon" and "orthopedic surgeon" that will include persons authorized to practice osteopathy and surgery, (*b*) "medical" and "practice of medicine" that will embrace the activities of osteopaths and (*c*) "medical college" that will include osteopathic schools; (2) in effect, to permit an osteopath to execute the examining physician's certificate required for admission to the Wisconsin general hospital or for commitment to governmental and private insane asylums, and (3) apparently to give all physicians, as defined, equal rights in the treatment of venereal disease. S. 192, to amend the medical practice act, proposes that "Applicants for license to practice osteopathy and surgery, after July 1, 1945, in addition to having a diploma from a reputable professional college approved and recognized by the board [of medical examiners], shall establish having completed a two years' college course including physics, chemistry, biology and either German or French, and if the professional college from which a diploma is presented does not require for graduation a hospital interneship of at least twelve months in addition to a four years' course, such applicant shall present a certificate that he has served at least twelve months interneship." S. 185 proposes that any person licensed before 1916 to practice osteopathy in the state is to have the right and privilege to exercise his professional judgment in the treatment of patients. The bill further provides that "Any license heretofore or hereafter issued [apparently referring to a license to practice osteopathy] shall legally qualify the holder for service in the capacity of physician under any statute of this state which provides for or permits the employment, appointment, election, or selection of a physician for any purpose whatever concerning health, service, or relating to health matters, without other recommendations by a professional society or association." S. 186 proposes that "Any sick or injured person entitled by statute or otherwise to the services of a physician, whose services for such person are to be paid for in whole or in part by said person's employer, or by some insurance carrier of such employer, or by any municipality, or by some society or association, or by some other person or persons, corporation, or partnership, shall be entitled to have the unrestricted and free choice of a physician to care for and administer to him." A. 392 proposes that "All employes in all state charitable and penal institutions shall be employed on the eight hour day basis." A. 401 proposes to authorize the incorporation of "associations . . . on a cooperative basis: 1. By individuals for the purpose of securing or paying for medical and hospital care for themselves and their families. 2. By a group of physicians for the purpose of providing medical and hospital care." Associations so formed are not to be subject to any of the insurance laws of the state. The bill also proposes to make it unlawful for any hospital, supported in whole or in part by public funds or wholly or partially exempt from taxation, to deny to any patient or any physician the facilities of such hospital because of affiliation with a cooperative association. The bill also proposes that no physician otherwise eligible for membership shall be excluded from membership in the state or county medical society because he enters into contracts with individuals or cooperative associations to furnish medical service on the basis of a stipulated sum to be paid periodically or because he is employed by an individual, a partnership or a cooperative association furnishing medical services on such terms. A. 411 proposes, in effect, to permit chiropractors to treat, at the expense of the employer, workmen injured in the course of their employment. The bill proposes to give the injured workman the right to "the attendance of any licensed chiropractor" and to require the employer to maintain a panel of licensed chiropractors ready to undertake the treatment of such of employees as may be injured.

WOMAN'S AUXILIARY

WINNERS IN THE HYGEIA CONTEST

The American Medical Association offered $150 in cash prizes to the county auxiliaries obtaining the largest number of subscription credits to *Hygeia* during December 1938 and January 1939.

The winners were:

Group I. Auxiliaries with a membership of from one to forty-nine:

$50 prize to Union County, Ark., Mrs. Warren S. Riley, Hygeia chairman, El Dorado, Ark.

Group II. Auxiliaries with a membership of from fifty to 199:

$50 prize to Berks County, Pa., Mrs. William F. Krick, Hygeia chairman, Reading, Pa.

Group III. Auxiliaries with a membership of more than 200:

$50 prize to Cook County, Ill., Mrs. W. J. Wanninger, Hygeia chairman, Chicago.

Honorable Mention was given to the following county chairmen:

Duval County, Fla., Mrs. Dan Funkenstein, chairman, Jacksonville, Fla.

Baldwin County, Ga., Mrs. C. H. Richardson, president, Milledgeville, Ga.

Labette County, Kan., Mrs. C. S. McGinnis, chairman, Parsons, Kan.

Ouachita Parish, La., Mrs. Henson Coon, chairman, Monroe, La.

Park Region District, Minn., Mrs. L. C. Combacker, president, Fergus Falls, Minn.

Washington County, Minn., Mrs. R. J. Josewski, chairman, Stillwater, Minn.

Albany County, N. Y., Mrs. F. E. Coughlin, chairman, Albany, N. Y.

Pottawatomie County, Okla., Mrs. R. M. Anderson, chairman, Shawnee, Okla.

Chelan County, Wash., Mrs. A. G. Young, chairman, Wenatchee, Wash.

Sheboygan County, Wis., Mrs. G. J. Hildebrand, chairman, Sheboygan, Wis.

Other counties that reached their quota were:

Mesa County, Colo.; Bulloch-Evans-Candler County, Ga.; St. Joseph County, Ind.; Shawnee County, Kan.; Wayne County, Mich.; Jackson County, Mo.; Burt-Dodge-Washington County, Neb.; Cayuga County, N. Y.; Guilford County, N. C.; Robeson County, N. C.; Elk-Cameron County, Pa.; Huntingdon County, Pa.; Lehigh County, Pa.; Mifflin County, Pa.; Montgomery County, Pa.; Westmoreland County, Pa.; Seventh District, South Dakota; Collingsworth-Childress-Hall County, Texas; Hunt-Rockwall-Raines County, Texas; Salt Lake County, Utah; Weber County, Utah; Clark County, Wash.; King County, Wash.; Pierce County, Wash.; Spokane County, Wash.; Walla Walla County, Wash.; Kanawha County, W. Va.; McDowell County, W. Va.; Rock County, Wis.; Washington-Ozaukee County, Wis.

The final result in this year's contest was 6,242 subscriptions, as against 4,747 received in the contest last year and 3,855 in 1937.

To the Hygeia chairmen, officers and members of the various county and state woman's auxiliaries who have assisted in making this contest a success, Mrs. James D. Lester, National Hygeia Chairman, expressed appreciation.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ARKANSAS

Sixth Graduate Course.—The Arkansas Medical Society presented its sixth course of graduate instruction at the University of Arkansas School of Medicine, Little Rock, January 31-February 1. In addition to clinics, papers were presented by Drs. David Harvey Shipp, Little Rock, "General Considerations of Empyema"; Herbert F. H. Jones, Little Rock, "Treatment of Ureteral Calculi"; Cyril M. MacBryde, St. Louis, "Effects Obtainable with Pituitary Gonadotropic and Sex Hormones"; Joseph F. Shuffield, Little Rock, "Internal Fixation of Fractures of the Neck of the Femur"; Frank D. Gorham, St. Louis, "Management of Peptic Ulcer," and David T. Hyatt, Little Rock, "Artificial Pneumothorax in the Treatment of Pulmonary Tuberculosis."

CALIFORNIA

County Society's Building Receives Honor Award.—The Southern California chapter of the American Institute of Architects recently awarded a certificate of honor to the Los Angeles County Medical Association "to recognize merit in design and execution of work in architecture and fine arts within its territory." The certificate records the chapter's belief that the library and assembly hall of the association deserve exceptional merit and its appreciation of the "sympathetic collaboration with the architect and the builder which made the building possible."

New Medical Laboratory at Stanford.—A new laboratory building has been given to Stanford University School of Medicine, San Francisco, by Mrs. Louis Stern, Palo Alto, in the name of her daughter Ruth Lucie Stern. The new unit will be used for research in cancer, neurology, infantile paralysis, childhood tuberculosis and other phases of pediatrics, certain types of fever and other public health problems, with special emphasis on neurology, in which the donor is chiefly interested. The three story building will be designed for workshop purposes without administrative offices or lobbies, and will contain thirty glass paneled workrooms.

DISTRICT OF COLUMBIA

Society News.—The Medical Society of St. Elizabeths Hospital will hold its second annual meeting in Washington April 14. The afternoon will be devoted to the presentation of papers. Guests will include Drs. Charles Macfie Campbell, medical director of the Boston Psychopathic Hospital and professor of psychiatry, Harvard University Medical School, Boston, and Riley H. Guthrie, newly appointed first assistant physician at St. Elizabeths Hospital. Further information may be obtained from Dr. Salomon Katzenelbogen at the hospital.

ILLINOIS

Society News.—Dr. Claude N. Lambert, Chicago, addressed the Stephenson County Medical Society at Freeport March 16 on "Fractures of the Hip."——At a meeting of the Lee County Medical Society in Dixon, March 16, Dr. Channing W. Barrett, Chicago, spoke on fibroids of the uterus.——Dr. Howard L. Alt, Chicago, discussed "Trends in Treatment of Diseases of the Blood" before the Sangamon County Medical Society in Springfield March 2.——Dr. Frank H. Lahey, Boston, presented the annual lecture of the Springfield Medical Club March 14, discussing gastrointestinal surgery. Mr. Charles C. Thomas, publisher of medical and scientific books and periodicals, spoke at this meeting on William Beaumont.

Chicago

The Luckhardt Lecture by DeKruif.—On April 12, Paul DeKruif, Ph.D., Holland, Mich., will speak at Mandel Hall of the University of Chicago, delivering the Arno Benedict Luckhardt Lecture of the Phi Beta Pi Fraternity under the title "Human Conservation."

Chicago's Health.—The general mortality rate for Chicago in 1938 dropped to an all time low of 9.7 deaths per thousand of population, a decrease of 6 per cent from the rate of 10.3 for 1937, according to a recent report. A new low point was established for infant mortality when thirty-four deaths of babies under 1 year of age per thousand live births were recorded; the maternal mortality rate dropped to 2.6 per thousand births, which, it was stated, was 25 per cent fewer deaths than in 1937. The city's birth rate was 14.3 per thousand of population, an increase over the rate for 1937, when it was 13.8. The total number of births was 51,500. The daily attendance at clinics throughout the city was 2,000, and more than 100,000 persons voluntarily took blood tests in the health department's campaign against syphilis.

Branch Meetings.—Dr. Irving S. Cutter addressed the Northwest Branch of the Chicago Medical Society March 17 at the Norwegian-American Hospital on "State Medicine—Present Trends in This Country." Discussion was opened by Drs. Morris Fishbein, Editor of THE JOURNAL, Rollo K. Packard and Nathan S. Davis III.——Dr. John M. Berger discussed "Acute Intestinal Obstruction, Diagnosis and Conservative Management" before the West Side Branch February 16, and Dr. George F. Thompson, the surgical treatment. ——Among others, Dr. J. Arnold Bargen, Rochester, Minn., addressed the Jackson Park Branch February 16 on "Constipation: The Mechanism of Production and Management."——A symposium on genito-urinary diseases dealing with infections of the upper urinary tract was presented before the Calumet Branch February 17 by Drs. William J. Baker, Andrew J. Sullivan and Dorrin F. Rudnick.——At a meeting of the Douglas Park Branch February 21 Dr. Harry A. Gussin spoke on "Proctology in General Practice."——Dr. Nathan S. Davis III discussed "Arteriosclerotic Heart Disease" before the Southern Cook County Branch February 21.

INDIANA

County Survey of Syphilis.—Lake County launched a survey of syphilis January 3 under the direction of the U. S. Public Health Service, the Indiana State Board of Health and the state medical society. The study aims to determine the number of cases in the county, the number of those not receiving treatment and those receiving adequate care. With Drs. Albert W. Ratcliffe and Wendell C. Kelly, Indianapolis, pathologist of the state department of health and chief of the state bureau of venereal diseases, respectively, as consultants, a county committee will carry out the work with the cooperation of physicians in the county.

KANSAS

Society News.—A symposium on acute otitis media was presented before the Sedgwick County Medical Society, Wichita, February 7, by Drs. Ernest E. Tippin, Orville C. McCandless, Charles L. Woodhouse, Hal E. Marshall, Earl D. Carter, Anthony F. Rossitto and Ernest M. Seydell, all of Wichita. ——The Shawnee County Medical Society was addressed January 9 by Drs. Orville R. Clark on "Acute Obstruction of the Ureter"; Arthur D. Gray, "Making Lantern Slides from 35 Mm. Film," and Archibald J. Brier, "Bacterial Sensitization in Relation to Other Allergic States." All are from Topeka.——Dr. Vern L. Pauley, Wichita, discussed "Renal Anomalies" before the Pratt County Medical Society, Pratt, January 27; Dr. Newman C. Nash, Wichita, spoke on "Carcinoma of the Uterus."——Dr. Lawrence S. Nelson, Salina, addressed the Clay County Medical Society January 18 on "Modern Treatment of Fractures of the Neck of the Femur." ——The Rice County Medical Society was addressed in Sterling January 26 by Dr. Joseph V. Van Cleve, Wichita, on "Fungus Diseases."

LOUISIANA

Exhibit of Medical Prints.—Two hundred medical prints are on display in the library of the Orleans Parish Medical Society, New Orleans, representing a part of the collection of Dr. Rudolph Matas. There are also photographs of the recent International Congress of Surgeons of which Dr. Matas was president.

Society News.—A symposium on recent advances in scleroderma was presented before the Orleans Parish Medical Society in New Orleans January 23 by Drs. James K. Howles, George E. Burch Jr., Edward W. Alton Ochsner and Michael E. DeBakey.——Dr. Isidore S. Kahn, San Antonio, Texas, discussed "Bronchial Asthma and Other Aspects of Allergy" before the East Baton Rouge Parish Medical Society recently. ——At a recent meeting of the Pointe Coupee Parish Medical Society in Morganza a round table discussion was held on infections of the hand.

MASSACHUSETTS

Another Doctors' Orchestra.—The Boston Doctors' Symphony Orchestra is being formed under the direction of Nicolas Slonimsky, according to the *New England Journal of Medicine*. All physicians, dentists and medical and dental students who are interested should communicate with Dr. Julius Loman, Pelham Hall Hotel, Brookline. Meetings began March 9 and will be held at Hampton Court Hotel, Brookline, every Thursday night.

The Dunham Lectures.—Dr. K. Linderström-Lang of the Carlsberg Laboratory, Copenhagen, delivered the following lectures at Harvard Medical School, Boston:

March 6, Micromethods for the Determination of Enzymes.
March 8, Distribution of Enzymes in Cells and Tissues.
March 10, Proteins and Proteolytic Enzymes.

This series is presented under the Edward K. Dunham Lectureship for the Promotion of the Medical Sciences.

Society News.—At a meeting of the Worcester District Medical Society in Worcester January 11 the speakers were Drs. Channing C. Simmons, Boston, on "Tumors of the Breast," and John T. B. Carmody, Worcester, "Injuries of the Peripheral Nerves"; Dr. Raymond H. Goodale, Worcester, showed a bacteriologic exhibit and slides of nonepithelial tumors of the breast.——The Boston Medical History Club was addressed January 9 by Dr. Edwin B. Dunphy on "Development of Knowledge of Diseases of the Eye."

New Position in Clinical Psychiatry.—Dr. John J. Slattery, acting superintendent of the state hospital at Medfield, has been appointed director of clinical psychiatry at the Boston State Hospital, a new position created by the legislature this year with an annual salary of $3,300 and maintenance. The director will have charge of all medical activities at the hospital. Under the former system the assistant superintendent was medical director in addition to handling administrative work. Dr. Slattery graduated at the Boston University School of Medicine in 1929.

MINNESOTA

Changes in Health Officers.—Dr. John A. McIntyre has been chosen health officer of Owatonna, succeeding the late Dr. Jerome F. Smersh.——Dr. Dennis M. O'Donnell has been appointed health officer of Ortonville.

Society News.—The Winona County Medical Society was addressed January 9 by Drs. Lewis G. Jacobs on "Therapy of Cancer of the Breast" and John A. Tweedy, both of Winona, on "Chronic Abdomen and Its Relation to the Abdominal Triad."——At a meeting of the Washington County Medical Society in January Dr. David Greth Gardiner, St. Paul, discussed bronchoscopy.

Six Day Graduate Courses.—A series of six day graduate courses in special fields of medicine recently started at the Center for Continuation Study of the University of Minnesota, Minneapolis. Following is the schedule:

Nervous and Mental Diseases, March 13-18.
Diseases and Injuries of Bones and Joints, March 13-18.
Diagnostic Roentgenology, March 27-April 1.
General Surgery, April 10-15.
Diseases of Blood and Blood Forming Organs, April 17-22.
Obstetrics, May 1-6.
Gastro-Enterology, May 8-13.

The programs are held in the special building devoted to graduate education for all professional fields. The building also serves as a residence hall for professional groups while they are attending the university. The tuition for each of the courses is $25, and room and board may be secured for $16. Physicians from outside of Minnesota are admitted on the same basis as residents. Further information may be obtained from J. M. Nolte, director, Center for Continuation Study, University of Minnesota, Minneapolis.

MISSOURI

District Meeting.—The Second Councilor District Medical Society will hold its second annual meeting at the Mark Twain Hotel, Hannibal, March 23. Dr. Morris Fishbein, Chicago, Editor of THE JOURNAL, will open the session by addressing a luncheon meeting of the chamber of commerce on "Frontiers of Medicine." Included in the scientific program will be:

Dr. Joseph C. Jaudon, St. Louis, Hypoglycemia of Infants and Children.
Dr. Howard A. Rusk, St. Louis, Diagnosis and Treatment of Chronic Undulant Fever.
Dr. Ernest Sachs, St. Louis, Present Status of Surgery of Brain Tumors and Some of the More Important Points of Diagnosis.
Dr. Evarts A. Graham, St. Louis, Primary Cancer of the Lung.

Speakers at the dinner will include Mr. Elmer H. Bartlesmeyer, St. Louis, executive secretary of the Missouri State Medical Association; Dr. James R. McVay, Kansas City, president-elect of the state association, and Dr. Fishbein, whose subject will be "American Medicine and the National Health Program."

Neuropsychiatric Meeting.—The Missouri-Kansas Neuropsychiatric Society met in Kansas City February 15 with the following speakers:

Dr. Edward T. Gibson, Kansas City, Thrombocytopenic Purpura, with Hemorrhage and Softening of the Spinal Cord.
Dr. Arthur Graham Asher, Kansas City, The Heart Before and After Metrazol Convulsions.
Dr. Ferdinand C. Helwig, Kansas City, Studies of the Brain in Delayed Death Following Strangulation.
Drs. Benjamin Landis Elliott, Robert Lee Hoffmann and Caryl R. Ferris, Kansas City, A Case of Hypertensive Encephalopathy.
Dr. Norman Reider, Topeka, Kan., Aphasia Following Exsanguination.
Dr. Harry Wilkins, Oklahoma City, Cerebellar Tumors: Their Diagnosis and Treatment.
Dr. Wallace Marshall, Appleton, Wis., Psychologic Observations with Reeducation in a Case of Multiple Sclerosis.
Dr. Theodore A. Watters, New Orleans, La., Fundamental Principles in Teaching Psychiatry.
Dr. Guy F. Witt, Dallas, Texas, Psychiatric Factors in Bromide Intoxication.
Dr. Lloyd H. Ziegler, Wauwatosa, Wis., Aspects of the Basic Science Underlying Clinical Neurology and Psychiatry.

Annual Spring Clinic.—The St. Joseph Clinical Society will hold its eighth annual two day spring clinic March 28-29 at St. Joseph. There will be no registration fee. The speakers will include:

Dr. Gershom J. Thompson, Rochester, Minn., Transurethral Prostatic Resection.
Dr. Quitman U. Newell, St. Louis, Cancer of the Uterus.
Dr. Fred J. Taussig, St. Louis (round table discussion), Treatment of Septic Abortion and Coordination of Radium with Surgery in the Treatment of Cancer of the Cervix.
Dr. Willis C. Campbell, Memphis, Tenn., Some Aspects of Surgery of the Hip Joint.
Dr. Heyworth N. Sanford, Chicago, Jaundice in the New-Born.
Dr. August A. Werner, St. Louis, Effect of the Ductless Glands in Growth and Development.
Dr. Ralph A. Kinsella, St. Louis, The Pneumonias.
Dr. Walter C. Alvarez, Rochester, Minn., Useful Hints in the Treatment of Indigestion.
Dr. Maurice C. Howard, Omaha, Neb., Problems of Gastric Hemorrhage.
Dr. J. Arthur Myers, Minneapolis, Modern Methods in Diagnosis and Therapy of Tuberculosis.
Dr. Coyne H. Campbell, Oklahoma City, Practical Points in the Management of Neurotic Symptoms, Inhibitions and Anxiety.
Dr. Manuel Grodinsky, Omaha, Pyogenic Infections of the Hand and Foot.

Dr. Sanford will speak at the banquet on disturbances of blood coagulation. Dr. Morris Fishbein, Chicago, Editor of THE JOURNAL, will speak at a noon luncheon on "American Medicine and the National Health Program" and will deliver a public address on "The Social Aspects of Medical Care."

NEW YORK

Personal.—Dr. John F. McNeill, assistant superintendent of Matteawan State Hospital, Beacon, has been appointed superintendent of the Institution for Male Defective Delinquents at Napanoch, it is reported.——Dr. Henry W. Lattin, Albion, was recently the guest of honor at the annual reunion of the Society of the Erie Canal in Albion. Dr. Lattin received a master pilot's license in 1880 when he was 21 and for several years before studying medicine operated steamers between Buffalo and New York.

Society News.—Dr. Allen O. Whipple, New York, addressed the Rochester Academy of Medicine March 1 on "Indications for and Results of Operations on the Spleen."——Dr. Willard M. Allen, Rochester, addressed the Rochester Pathological Society March 16 on "Types of Glandular Unbalance Frequently Seen."——Dr. Hugo Roesler, Philadelphia, conducted courses on heart diseases and demonstrations of fluoroscopic examination of the heart and aorta in Syracuse February 3-5 and 10-12 under the auspices of the Onondaga County Medical Society.——Dr. William Thalhimer, New York, addressed the Medical Society of the County of Nassau, Garden City, February 28, on "Prophylactic and Therapeutic Uses of Convalescent Measles and Convalescent Scarlet Fever Serums."——A Joint Committee in Specialties, comprising pathologists, radiologists, anesthetists and physical therapists has been formed in New York with Dr. Maxwell J. Fein, Brooklyn, as chairman and Dr. Madge C. L. McGuinness, New York, as secretary. About 1,500 members of the Medical Society of the State of New York are represented.

New York City

Heart Association Honors Dr. Conner.—Directors of the American Heart Association recently voted to name an annual lecture established last year the Lewis A. Conner Lecture in honor of Dr. Conner, who was the first editor of the *American Heart Journal* and the first president of the association. The lecture will be given during the annual meeting in St. Louis May 12-13.

Hospital News.—Parkway Hospital at 123 West One Hundred and Tenth Street has been taken over by the Italian Hospitalization Society to be operated for the Italian community on a nonprofit basis. The society was established in 1937.——Dr. Paul Liebesny, formerly director of the physicomedical section of the Physiologic Institute in the Allgemeine Krankenhaus, Vienna, has been appointed director of the physical therapy department of the Bronx Hospital.

Dr. Thygeson Succeeds Dr. Wheeler at Columbia—Dr. Dunnington Promoted.—Dr. Phillips Thygeson, assistant professor of ophthalmology at Columbia University College of Physicians and Surgeons since 1936, has been promoted to a full professorship and appointed executive officer of the department of ophthalmology to succeed the late Dr. John M. Wheeler. Dr. Thygeson is 35 years old and graduated from Stanford University School of Medicine, Stanford University, Calif., in 1928. In 1931-1932 he held a National Research Council fellowship in medicine, working on trachoma at the Pasteur Institute in Tunis. Announcement was made at the same time of the promotion of Dr. John H. Dunnington, associate professor of ophthalmology, to a full professorship. Dr. Dunnington graduated from the University of Virginia Medical Department in 1915 and has been assistant director of the Institute of Ophthalmology, Presbyterian Hospital, since 1933.

Courses for New Library Technics.—The School of Library Service at Columbia University announces two new courses to be given during the summer session, one on microphotography and one on bibliographic and reference service in the medical sciences. The course on microphotography is designed to meet the need which libraries are now facing for skilled service in the production and use of microfilms as a substitute for the printed page or original documents, according to the announcement. A new laboratory is now under construction for the course, which will consist of daily lectures and two laboratory periods a week. Registration for laboratory work is limited to twenty students to be selected from applications received before June 1. The course in medical library service will be given by Mr. Thomas P. Fleming, librarian of the Columbia University Medical Library. If the response is satisfactory, it will be given regularly in the summer session and possibly also in the spring session after 1940. Besides reference and bibliographic work, it will include indexing, abstracting and reviewing medical journals.

NORTH CAROLINA

Health Officer Honored.—Dr. Joseph A. Morris, Oxford, who recently retired as health officer of Granville County after about twenty years of service, was honored at a testimonial dinner February 16, given by the Granville County Medical Society, the Rotary and Kiwanis clubs and the Young Men's Club. Among the speakers were Dr. Robert E. Fox, Raleigh, director of county health work for the state board of health and State Supreme Court Justice W. A. Devin, Raleigh. The group presented a watch to Dr. Morris.

Society News.—Dr. William D. Hall, Raleigh, was elected president of the North Carolina Neuropsychiatric Society at its annual meeting at the Caswell Training School, Kinston, January 27; Dr. William Ray Griffin, Asheville, was elected vice president and Dr. Malcolm D. Kemp, Pinebluff, reelected secretary.——Dr. Joseph Stokes Jr., Philadelphia, addressed the Guilford County Medical Society, Greensboro, February 9, on "Newer Advances in Infectious Diseases, Particularly Respiratory Diseases." Dr. Louis L. Hobbs Jr., Ridgeway, Pa., addressed the society January 5 on "Goiter, Its Clinical, Surgical and Pathological Aspects." —— Dr. William L. Kirby, Winston-Salem, addressed the Davidson County Medical Society, Lexington, January 11, on allergy in relation to dermatology.

OHIO

State Board Officers Elected. — Dr. Louis T. Franklin, Chillicothe, was elected president of the State Medical Board of Ohio at a meeting January 17. Dr. John H. J. Upham, Columbus, was elected vice president and Dr. Herbert M. Platter, Columbus, reelected secretary.

Funds for Research on Dementia Praecox. — The National Committee for Mental Hygiene recently granted $1,000 to Longview State Hospital, Cincinnati, to continue research on dementia praecox under Drs. Esther Bogen Tietz and Douglas Goldman. The funds for this work were contributed by the Committee on Research on Dementia Praecox founded by the Supreme Council, Scottish Rite Masons, Northern Jurisdiction.

OREGON

Changes in State Health Board.—Drs. Harvey A. Woods, Ashland, and Wendell H. Hutchens, Portland, were recently appointed new members of the state board of health and Drs. Arthur W. Chance, Portland, and Norman E. Irvine, Lebanon, were reappointed. Dr. Frank Mount, Portland, was elected president at a meeting January 10; Dr. William J. Weese, Ontario, vice president, and Dr. Frederick D. Stricker, Portland, executive secretary and state health officer.

PENNSYLVANIA

Society News. — Dr. Harold W. Jones, Philadelphia, addressed the Cambria County Medical Society, Johnstown, February 9 on "Treatment of Diseases of the Blood." —— Dr. Harold L. Foss, Danville, addressed the Northampton County Medical Society February 17 at the Country Club of Northampton County on "Treatment of Advanced Thyrotoxicosis."——Dr. Joseph H. Barach, Pittsburgh, addressed the McKean County Medical Society, Bradford, January 17 on "Nutritional Requirements in Diabetes." —— Dr. Murray M. Copeland, Baltimore, addressed the Washington County Medical Society, Washington, March 8 on "Diagnosis and Treatment of Tumors of the Breast."

RHODE ISLAND

Special State Meeting.—Dr. Rock Sleyster, Wauwatosa, Wis., President-Elect of the American Medical Association, addressed a special meeting of the Rhode Island Medical Society in Providence January 6, describing the development of American medicine and the work of the American Medical Association.

SOUTH CAROLINA

State Society Entertains General Assembly.—The South Carolina Medical Association entertained the members of the general assembly and Governor Maybank at a luncheon at the Columbia Hotel, Columbia, January 25. Preceding the luncheon Dr. Reginald Fitz, Boston, addressed the legislators on trends in medical education.

State Pediatric Meeting.—Dr. Daniel Lesesne Smith Jr., Spartanburg, was elected president of the South Carolina Pediatric Society at its annual meeting in Columbia January 23. Dr. Lonita M. Boggs, Greenville, was elected vice president and Dr. William Weston Jr., Columbia, secretary. Dr. Martha M. Eliot of the Children's Bureau, U. S. Department of Labor, Washington, D. C., was the guest speaker on "The Maternal and Child Health Program Under the Social Security Act."

UTAH

Annual Registration Due April 1.—All practitioners of medicine and surgery licensed to practice in Utah are required to register annually on or before April 1, with the Department of Registration and to pay a fee of $3. If a licentiate fails to reregister within from ninety days to six months after April 1, his license can be revoked, and if revoked it will be reinstated thereafter only on his paying the delinquent registration fees and an additional year's fee as a penalty.

WASHINGTON

Personal.—About seventy-five friends and colleagues honored Dr. Nils A. Johanson, Seattle, with a stag party February 9, on the thirtieth anniversary of the founding of the Swedish Hospital by Dr. Johanson. It was also a farewell party to Dr. Johanson, who is leaving for New Guinea.

WISCONSIN

Pneumonia Control Committee Appointed. — At the request of the state board of health, the council of the State Medical Society of Wisconsin has authorized appointment of a committee to confer with the board on the formulation of a program for control of pneumonia. The members are Drs. Arthur J. Patek, Milwaukee; Thomas J. Snodgrass, Janesville, and Alvin G. Koehler, Oshkosh.

Society News.—Dr. Armand J. Quick, Milwaukee, addressed the Racine County Medical Society, Racine, February 16 on "Value of Prothrombin Determination and Hippuric Acid Test in the Study of Jaundice Patients."——Dr. Stephan Epstein, Marshfield, addressed the Wood County Medical Society, Marshfield, February 21, on "Differential Diagnosis and Treatment of Benign Skin Tumors."——Dr. Elmer L. Sevringhaus, Madison, discussed endocrinology at a meeting of the Columbia-

Marquette-Adams County Medical Society in Portage February 21.——Drs. John L. Emmett and Horton C. Hinshaw, Rochester, Minn., addressed the Chippewa County Medical Society, January 24, on "Management of Urinary Calculi" and "Recent Advances in the Treatment of Pneumonia" respectively.——Dr. Reginald Jackson, Madison, addressed the Dane County Medical Society, Madison, January 10, on "Surgery of the Colon."

WYOMING

Annual Registration Due April 1.—All practitioners of medicine and surgery licensed to practice in Wyoming are required by law to register on or before April 1, with the secretary of the Board of Medical Examiners and to pay a fee of $2.50. If a licentiate fails to pay the fee within three months after April 1, his license can be annulled, and if annulled it will be reinstated only on his paying the stated fee, plus $5 as a penalty.

GENERAL

Society News.—Dr. L. Fernald Foster, Bay City, Mich., was chosen president of the Northwest Regional Conference at its session in Chicago February 12.——Dr. M. Pierce Rucker, Richmond, Va., was named president-elect of the South Atlantic Association of Obstetricians and Gynecologists at its first annual meeting in Charleston, S. C., February 11. Dr. Robert E. Seibels, Columbia, S. C., became president and Dr. Robert A. Ross, Durham, N. C., was reelected secretary. The association was organized a year ago at a meeting in Charlotte, N. C. The next meeting will be in Richmond, Va., in 1940.

Pacific Coast Surgeons to Meet.—The annual meeting of the Pacific Coast Surgical Association will be held in San Francisco and Del Monte, Calif., March 28-31. The tentative program includes the following speakers:

Dr. Frank Hinman, San Francisco, Cancer of the Prostate.
Drs. Maurice G. Kahn and Howard F. West, Los Angeles, Adenoma of the Pancreas.
Dr. Andrew A. Matthews, Spokane, Cancer of the Breast.
Dr. Thomas F. Mullen, San Francisco, Safeguarding the Unconscious Operative Patient.
Dr. Paul G. Flothow, Seattle, Advances and Retreats in Neurosurgery.
Dr. Millard T. Nelsen, Tacoma, The Surgical Anatomy of Fistula-in-Ano.

Dr. Sumner Everingham, Oakland, is president of the association.

Prevalence of Communicable Disease.—The U. S. Public Health Service recently announced that for the first six weeks of 1939 20,877 cases of influenza were reported as compared with 18,420 for the corresponding period of 1938. The number of deaths from pneumonia for a group of cities with a total population of about 33,000,000, was 762 for the week ended February 4 as compared with a five year average of 992. Smallpox was reported to be unusually prevalent in Indiana (308 cases), Ohio (126), Iowa (117), Kansas and Minnesota (97 cases each), Oklahoma (94), Arizona (83), California (71) and Texas (65) during January. More than two thirds of the total number of cases (1,548) for the whole country occurred in these nine states. The total was about 65 per cent of last year's figures.

Prize for Thesis in Obstetrics.—The American Association of Obstetricians, Gynecologists and Abdominal Surgeons again offers its annual Foundation Prize for a thesis. The prize this year will be $100. Those eligible to compete are (1) interns, residents or graduate students in obstetrics, gynecology and abdominal surgery, and (2) physicians who are actually practicing or teaching obstetrics, gynecology or abdominal surgery. Competing manuscripts must be presented in triplicate under a nom de plume to the secretary of the association before June 1, must be limited to 5,000 words and such illustrations as are necessary for a clear exposition of the thesis and must be typewritten (double spaced) on one side of the sheets, with ample margins. The successful thesis must be presented at the annual meeting of the association in September without expense to the association and in conformity with its regulations. For further details address Dr. James R. Bloss, Secretary, 418 Eleventh Street, Huntington, W. Va.

Pacific Science Congress in San Francisco.—The sixth Pacific Science Congress will be held in California July 24 to August 12 under the auspices of the National Research Council. Sessions will be held at the University of California, Berkeley, Stanford University and in "Pacific House" on the grounds of the Golden Gate International Exposition in San Francisco. The theme of this congress will be "the present stage of knowledge of Pacific problems and methods by which that knowledge may be most profitably enlarged," and the program will be arranged as a series of symposiums. Among them are one on "Communicable Diseases of the Pacific Area; Origin, History, Distribution; Tropical Medicine" and one on "Nutritional Problems of the Pacific Area." Information about the congress may be obtained by addressing the secretary-general, Roy E. Clausen, Ph.D., Room 205 Hilgard Hall, University of California, Berkeley. The last previous congress in this series was in Vancouver and Victoria, B. C., in 1933.

Physicians' Art Exhibition.—The American Physicians' Art Association will hold an exhibition of art by members at the City Art Museum of St. Louis, May 14-30. Works in any of the fine or graphic arts are eligible. The privilege of exhibiting works is open to members of the American Physicians' Art Association, to honorary members and to other physicians, dentists and doctors of philosophy, by invitation. All works submitted must be appropriately framed. Foreign exhibitors, however, might well have their art pieces framed in this country, as picture frames are taxed on entrance, whereas unframed pictures are not taxed. Not more than five works will be accepted from any one entrant. The hanging fee is one piece $2, two pieces $4, three pieces $5 and five pieces $7. The check should be made out to Dr. R. W. Burlingame, treasurer, and mailed with entry notice to Miss Dorothy Hetlage, City Art Museum, St. Louis, Mo. No entries will be received after 5 p. m. May 1. Prizes, medals and cups will be be awarded.

Government Services

National Cancer Institute Buys Radium

The National Cancer Institute purchased in December 9.5 Gm. of radium valued at $200,000. The radium supply will be lent to hospitals and clinics for treatment of cancer. An institution that borrows the radium must take the responsibility of transporting it from the Bureau of Standards and back again for periodic testing, must store it properly while using it and must insure it against loss and damage. According to the *Health Officer*, personnel and equipment of the borrowing institution must meet standards equal to those established by the American Board of Radiology for the safe use of radium. According to the terms of the loan, preference in use of the radium will be given to persons unable to pay for treatment.

Examination for Medical Officers in Veterans' Administration

The U. S. Civil Service Commission announces an open competitive examination for the position of associate medical officer in the Veterans' Administration with a salary of $3,200 a year. Competitors will not be required to report for written examination but will be rated on the extent of their education and on their experience and fitness. If conditions permit, an oral examination will be given to a sufficient number of competitors in the order of their standing to meet the needs of the service. Applicants must not have passed their fortieth birthday on the closing date for applications. They must have graduated from a recognized medical school since May 1, 1934, and must have completed at least one year of internship. Persons now serving internships may apply but cannot be appointed until proof of satisfactory completion of the internship is furnished. Detailed information and application forms may be obtained from the secretary of the U. S. Board of Civil Service Examiners at any first class postoffice, from the commission at Washington or from the civil service district office at any of the following cities: Atlanta, Boston, Chicago, Cincinnati, Denver, New Orleans, New York, Philadelphia, Seattle, St. Louis, St. Paul, San Francisco, Honolulu, Balboa Heights, C. Z., and San Juan, P. R. The closing date is April 10 except from the following states, for which the date is April 13: Arizona, California, Colorado, Idaho, Montana, Nevada, New Mexico, Oregon, Utah, Washington and Wyoming.

CORRECTION

Evanston Hospital's Necropsy Percentage.—Evanston Hospital, Evanston, Ill., should have been included in the list of approved internship hospitals having over 70 per cent necropsies on page 924 of the Hospital Number of THE JOURNAL, March 11, 1939. Its record was 81.2 per cent.

Foreign Letters

LONDON

(From Our Regular Correspondent)

Feb. 18, 1939.

Epidemic Nausea and Vomiting

In 1935 Danish writers described under the name of epidemic nausea what appears to be a new disease. They meant by nausea not simply the feeling of sickness but all the symptoms of sea sickness. In 1936 the disease was first observed in England in a boarding house for girls at the seaside resort of Broadstairs by the pediatrician Reginald Miller and M. O. Raven. It affected fifty-two of 117 residents. Miller described the disease in the "Proceedings of the Medical Officers of Schools Association":

The chief symptoms are vomiting, nausea, giddiness and diarrhea. Vomiting occurred in forty-two of the fifty-two cases. It was often explosive and unexpected; in many cases it was a single vomit only and tended to occur on the patient's waking in the morning. In no case did the sickness last more than six hours. Nausea without vomiting occurred in ten cases and giddiness in thirteen. Diarrhea did not occur. The disease seemed clearly of the same type as the Danish epidemics but there were certain differences. In the first Danish epidemic mild diarrhea with mucus in the stools occurred toward the end of the illness in twelve of forty-seven cases. In the second also diarrhea occurred, but it is particularly mentioned that no blood or mucus was present in the stools. Fever was rare and always slight. Recovery was complete in forty-eight hours. The epidemic affects persons of all ages but has a tendency to spare infants. A characteristic is the high proportion of a population attacked (from 33 to 75 per cent). The cause is obscure. Miller regards it as air borne and probably infectious.

Other epidemics have been observed in England. The last was reported by J. D. Gray (*Brit. M. J.* **1**:209 [Feb. 4] 1939). It occurred in a country district (South Hampshire). In addition to the vomiting, frontal headache, diarrhea, pyrexia (the temperature always below 100 F.) and occasionally bradycardia were observed. In a girls' school forty-five of eighty-two pupils were attacked, and at the same time the disease was prevalent in the surrounding country. No organisms known to cause gastro-enteritis were found. The greatest argument against food or water contamination was the type of spread in families or institutions from the first patient. Thus two of the school children went home and two days later both parents contracted the disease. Sonne dysentery in an institution might be confounded with epidemic vomiting but is distinguished by its much greater severity.

Thrombosis Following Injection of Iopax (Uroselectan)

Though mishaps occur from time to time in the injection of veins, a case in which the surgeon has to defend himself against a charge of negligence has only now arisen. A woman aged 52 was given an injection of iopax (uroselectan) for x-ray examination of the kidneys by the house surgeon of the Kent and Canterbury Hospital in December 1934. He first tried to inject the substance into the veins of the arms but could not do so because these veins were not visible. He then found a suitable vein in the left leg, which he injected. This was the only occasion on which he saw the woman. A roentgenogram taken seven minutes after the injection clearly showed the pelvis of the kidney. She alleged that the injection was so negligently performed that some of the fluid escaped into the tissues around the vein and gave rise to phlebitis, the consequence of which was disability likely to be permanent. She suffered much pain and when she returned home had to go to bed, where she remained under medical care for six months. In his evidence the surgeon stated that he had successfully injected this drug on many occasions. When he injected the plaintiff's vein the needle was in the vein. Pain was commonly caused, but he had no recollection of any unusual complaint on her part. Medical evidence was given that thrombosis might result when the injection was made into the vein and that some people had a tendency to thrombosis, the reason for which was not known. The judge said that there was no evidence that the surgeon had done anything that he ought not to have done or that there was any lack of skill on his part. He therefore gave judgment for the defendant.

The British Heart Journal

A new periodical, the *British Heart Journal*, has been inaugurated by the British Medical Association. It is under the control of an editorial board of cardiologists. In a foreword Sir Thomas Lewis states that the Cardiological Society of Great Britain has decided to have a journal of its own. He points out that there is no stronger tradition of work on the heart than the British, which begins with the incomparable Harvey and passes through Lower, Hales, Heberden, Stokes, Mackenzie and other clinicians as well as the physiologists Gaskell and Starling. The *Journal* is to be published quarterly and the subscription fee is $5 to members of the society and $6 to nonmembers. The January issue, which has just been published, contains "Some Disturbances of the Rhythm of the Heart," by John Cowan; "Digitalis in Heart Failure with Normal Rhythm," by C. J. Gavey and John Parkinson; "Chest Leads in Clinical Electrocardiography," by Paul Wood and Arthur Selzer; "A New Sign of Left Ventricular Failure," by Paul Wood and Arthur Selzer; "The Significance of Electrocardiograms Showing a Second Positive Wave of QRS in Lead III," by A. A. Fitzgerald Peel, and "Some Notes on the Cardiac Club," by John Cowan and others.

PARIS

(From Our Regular Correspondent)

Feb. 11, 1939.

Blood Transfusion During War

Several years ago a committee composed of Profs. A. Gosset, E. Levy-Solal and Arnault Tzanck was appointed to elaborate a technic for blood transfusion on a large scale which might be applied in case of war. This committee submitted its report at

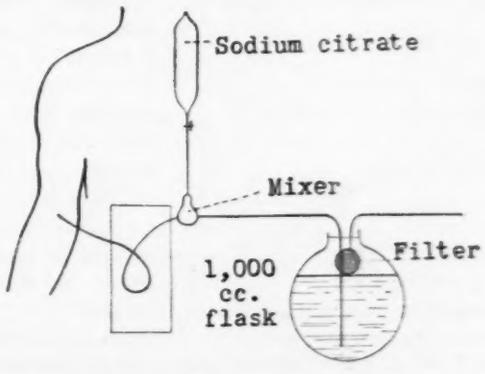


Fig. 1.—Henry-Jouvelet apparatus.

the February 7 meeting of the Académie de médecine of Paris. The recent experience of countries at war in Europe and Africa has shown that no matter how thorough the prewar preparations for transfusions have been they are usually found to have been inadequate. At least 60 liters of blood must be ready for imme-

diate use in each of the main centers and subcenters. This means that only conserved refrigerated blood can be considered as practicable, because of the necessity of transporting it to the first aid stations. This amount of blood must be furnished by noncombatants relatively far behind the front and ought not to be furnished either by soldiers or by hospital personnel. The blood should be ready to be used, having been conserved in simple sterilized flasks, such as are employed for conserving ordinary serum. All laboratory examinations are made at the chief or subcenters, each donor giving from 300 to 500 cc., which is collected in a 1,000 cc. flask. The apparatus which the committee recommended is that of Henry and Jouvelet,

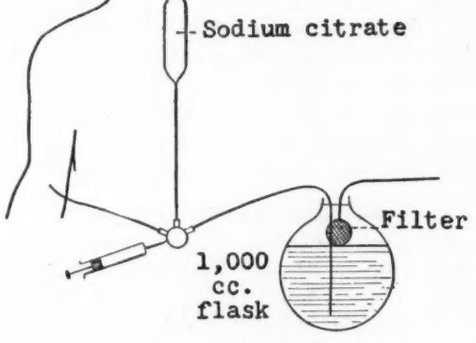


Fig. 2.—Tzanck three way distributer.

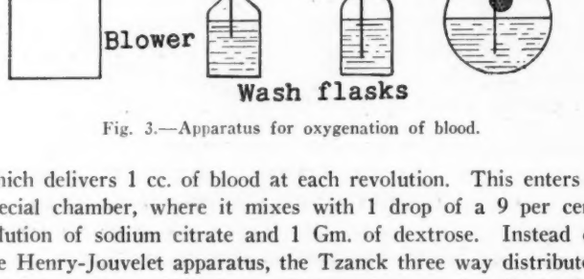


Fig. 3.—Apparatus for oxygenation of blood.

which delivers 1 cc. of blood at each revolution. This enters a special chamber, where it mixes with 1 drop of a 9 per cent solution of sodium citrate and 1 Gm. of dextrose. Instead of the Henry-Jouvelet apparatus, the Tzanck three way distributer can be used, in which 1 cc. of citrated serum is mixed with every 10 cc. of blood. Although not absolutely necessary, oxygenation of the blood is of great aid, because it indicates absence of infection if the blood retains its red color. After 1,000 cc. of citrated blood has been collected, the flask is inverted and its contents are allowed to run into four flasks, each with a capacity of 250 cc. Each 250 cc. flask is placed in a cardboard box, well covered by corrugated paper, so that the blood will retain its low temperature after it is taken out of the refrigerator. For transportation an airplane or fast motor vehicle with refrigeration equipment is to be preferred to a train and six flasks are placed in a single corrugated cardboard box. Instead of a simple 250 cc. flask, one with a marked constriction at the center is now being used in the Spanish armies to eliminate, so far as possible, shaking of the blood during its transportation to the front. As to injection, the citrated blood is allowed to flow by gravity into the vein of the recipient through a sterilized rubber tube and needle, which traverse a dish filled with water at 39 or 40 C. At least six mobile laboratory units should be available, which can function in some city well behind the front. To make possible the securing of 60 liters of blood, the unit should be established in a community where at least 30,000 potential donors can be examined. Such units ought really to be established in the larger cities in peace time, so that they would be ready to function when war broke out. This has already been done in France, each civilian donor being given an identity card after the necessary laboratory examinations.

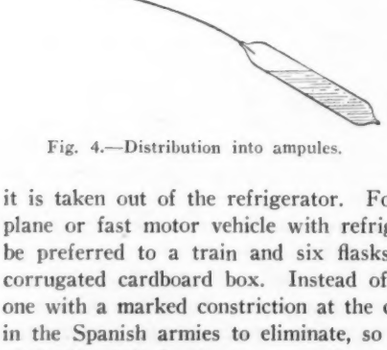


Fig. 4.—Distribution into ampules.

The personnel of the chief and secondary centers ought to be provided for in peace time. The physician in charge of the center, the laboratory head and the assistants should be persons who are exempt from mobilization and who have had ample experience in the collection of blood for transfusion purposes. The slightest error made by a technician may be followed by disastrous results. Although citrated conserved blood is indispensable when large quantities are needed, one must not overlook the fact that noncitrated blood, i. e. pure blood, is to be given preference when available or when transportation of citrated blood to the front is impossible. Technicians ought to be trained during peace time so as to be available in war. At the Paris center more than 150 technicians have been given a thorough course of instruction.

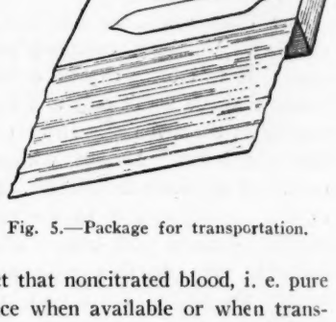
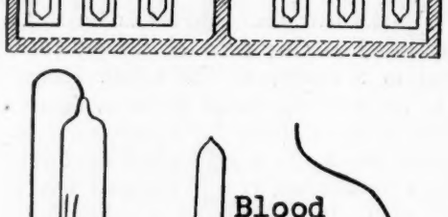


Fig. 5.—Package for transportation.



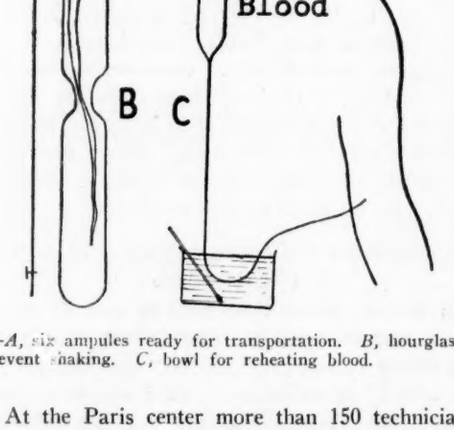


Fig. 6.—*A*, six ampules ready for transportation. *B*, hourglass ampule, used to prevent shaking. *C*, bowl for reheating blood.

A Proposed Health Record for Every Citizen

Several years ago the minister of public health gave orders that a study be made as to the practicability of every person's possessing a book in which all illnesses and injuries are to be recorded, so that a physician who is called to treat a man, woman or child will immediately have at his disposal much valuable information as to the previous medical history. Objec-

tions were raised that the recording of venereal infections would be resented; hence but little progress was made until recently, when the present minister of public health appointed a physician who has had a large experience in the French colonies to study the advisability of a health book, or "carnet de santé," which would be obligatory for every person in European France and its colonies. It has been proposed to eliminate the previous objection to the recording of venereal disease by the use of some secret initials or nomenclature which can be interpreted only by physicians.

BERLIN

(From Our Regular Correspondent)

Jan. 30, 1939.

The Genetic Aspect of Diabetes Mellitus

Extensive studies of the hereditability of diabetes mellitus in an unselected group of twins heretofore have not been available. Research is now being carried on by Hildegard Then Berg at the Kaiser-Wilhelm Institute of Genealogy and Demography, Munich. Then Berg began with a basic material of some 85,000 persons with diabetes mellitus, among whom there were 411 pairs of twins, and she has already studied 147 of these pairs. Forty-six were enzygotic and eighty-seven were dizygotic; the exact zygotic origin of two pairs was open to question, and the remaining twelve pairs had to be eliminated from the study, since they presented no diabetes mellitus whatever. The author tries to observe all the twins personally. She examines the urine and blood sugar and in most cases performs a blood sugar tolerance test. A pair of twins is termed "absolutely concordant" if each twin of the pair was at the time of examination suffering from a manifest diabetes mellitus with demonstrable excretion of sugar in the urine. If one twin, although not manifestly ill and passing normal urine, shows by the tolerance test that the insular system is unable to metabolize a tolerance test dose of twice 20 Gm. of dextrose, the pair is termed concordant according to tolerance. A group termed discordant according to tolerance is also distinguished; among these the dextrose tolerance test of the twin who is not manifestly ill reveals a normal blood sugar curve, which (after fasting) is not above 120 mg. per hundred cubic centimeters. This curve, furthermore, at its peak does not exceed 180 mg. per hundred cubic centimeters; in the second tolerance test with dextrose (after forty minutes) it shows no further rise, and finally, after 120 minutes, it returns to its normal value. Termed probably discordant are those pairs of twins who could not be examined because they had already died but who, according to the histories of their cases, appear not to have been affected with manifest diabetes mellitus.

According to the figures thus far elicited from these carefully performed studies, seventeen pairs of enzygotic twins were absolutely concordant, thirteen were concordant according to tolerance, six were discordant according to tolerance and ten were probably discordant; nine pairs of dizygotic twins were absolutely concordant, nine were concordant according to tolerance, thirty-two were discordant according to tolerance and thirty were probably discordant. Then Berg established an interesting correlation between manifest diabetes mellitus and age. It was found that almost without exception after the age of 43 the enzygotic pairs were all concordant, and not one discordant pair was to be observed above this age limit.

It is therefore proved on the basis of a large group of twins that diabetes mellitus is purely hereditary; it is possible, however, with the examination methods available, to establish certain proof of the inherited inferiority only if the twins have passed the forty-third year of life.

Immediate Resection in Cases of Perforating Gastric Ulcer

The therapeutic results with freely perforating gastric and duodenal ulcers have been considerably bettered in the last fifty years. The mean mortality in earlier times was as high as from 60 to 90 per cent, but in the last decade it has decreased to below 20 per cent. Information on this topic has recently been compiled by Dr. Junghanns at the surgical clinic of Frankfort University (Professor Schmieden's clinic). Whereas formerly only 16 per cent of the patients came to operation during the first six hours and 54 per cent during the first twelve hours following perforation, in the last ten years 75 per cent came to operation during the first six hours after perforation and 95.4 per cent within the first twelve hours.

Moreover, changes in the surgical technic have made possible a more favorable prognosis. Immediate gastric resection has supplanted the older palliative interventions (suturing over, with or without gastro-enterotomy). In the last ten years there were performed at the Schmieden clinic sixty gastric resections (second method of Billroth), with a mortality of 6.7 per cent, and fifty-one palliative operations, as mentioned, with a mortality of 39.2 per cent. More favorable results can be obtained if the general condition, the circulation in particular, is correctly evaluated. The time elapsed between perforation and intervention is therefore not the decisive factor. Immediate resection has the additional advantage of leading to essentially more favorable permanent results. Follow-ups disclosed that 95.8 per cent of the patients who submitted to resection were completely fit to work, whereas only 67.8 per cent of those who had undergone palliative operations had regained complete working capacity.

Indications for Arteriography and Ventriculography

The neurosurgeon Professor Tönnis recently discussed the indications for arteriography and ventriculography before the Berlin Medical Society. X-ray examination by means of ventriculography has become an important procedure for neurosurgeons, despite the fact that a mortality of 8 per cent is still to be reckoned with. A great many brain tumors and other cerebral disorders could not be diagnosed without ventriculography, and conditions of this sort incorrectly diagnosed almost invariably result in a fatal outcome. Insufflation of the ventricle, which is generally done after suboccipital puncture, makes possible an exact evaluation of the site, size and type of any tumor relating to the ventricles. Cases in which a considerable elevation of cerebral pressure is present are unsuitable for ventriculography. Consequently, arteriography has come increasingly to the fore. In the latter method the exposed internal carotid is injected with thorium dioxide sol. In this way information with regard to tumors of the medial or anterior cranial fossae is elicited without exposing the patients to the danger of increased cerebral pressure. Tumors of the temporal lobe can be visualized readily by this means. Since the region of the posterior cranial fossa is not supplied by the internal carotid artery, tumors arising there cannot be diagnosed by arteriography. The method is particularly valuable because it not only makes possible conclusions with respect to the site of the tumor but shows the source of the neoplasm's vascular supply as well. Since by arteriography tumors can be differentiated according to their richness or poverty in vasculature, accurate diagnoses with regard to their histologic structure may be made. The procedure is of special importance for the diagnosis of meningiomas and multiform neoplasms. It also aids in the recognition of brain abscesses and subdural hematomas. Ventriculography as well as arteriography should be done only if the indication is definite and then only by a specialist skilled in the technic.

POLAND

(From Our Regular Correspondent)

Feb. 1, 1939.

A Clinical Study of Angina Pectoris

Dr. M. Semerau-Siemianowski, professor at Warsaw University, and Dr. H. Rasolt have published a study of angina pectoris based on 518 patients seen by Professor Semerau-Siemianowski in his private practice and on eighteen patients admitted to the St. Lazarus Hospital in Warsaw. These 536 patients were observed between 1925 and 1933. In 1936 a follow-up letter was sent to every patient. The small number of patients admitted to the hospital in proportion to those seen in private practice agrees with the records of others.

The ratio between the number of patients with angina pectoris and all patients over 20 with cardiovascular disorders consulted during the same period was 518 to 4,373, i. e. 12 per cent. White in America found the percentage to be 12.5, Koller in Germany 8.1, and J. Pawiński in Poland 5.2. According to Cabot, cardiovascular disease occurs in 38 per cent of all patients; then the actual incidence of angina pectoris in Poland could be estimated at about 4.6 per cent of all other diseases. The incidence of angina pectoris obtained in the same way from the statistical data of White is 4.75 per cent, while in the former (1913) Polish report of Pawiński it was but 2.9. Thus there was an increase in the incidence of angina pectoris in Poland during the last two decades. Furthermore, this increase was more marked in the later four years of the period considered, 1929-1932, than in the former four years, 1925-1929. This applies particularly to the organic forms of angina pectoris. Professor Semerau-Siemianowski supposes that this rise in the angina pectoris incidence may be due partly to social factors.

According to Professor Semerau-Siemianowski there are two main types of this disease, the organic and the functional. In the former he has distinguished two main forms: the acute form consists of only one variety, the cardiac infarction. The chronic form has three varieties: coronalgia, attributed to changes in the main coronary arteries and occurring with the clinical picture of angina of effort; myocardialgia, attributed to diffuse changes of the minute coronary arteries, followed by small necrotic foci in the myocardium and characterized by slight attacks of cardiac pain occurring at rest and by coexisting signs of heart failure, and aortalgia, due to pathologic changes in the aorta. There are four varieties of so-called functional angina pectoris: (1) the neurotic variety; (2) reflex angina pectoris, the attack being provoked by disorders in other organs, e. g. by flatulence or gallbladder diseases; (3) toxic angina, attributed to nicotine, caffeine or such endogenic factors as gout and endocrine disorders, and (4) anemic angina pectoris, caused by myocardial ischemia without any coronary disease.

The incidence found for these varieties of angina pectoris was coronalgia 52.7 per cent, aortalgia 11.5 per cent, myocardialgia 6.8 per cent and cardiac infarction 7.7 per cent. The organic forms of angina pectoris were found in 78.7 per cent of cases and the functional forms in 21.3 per cent. Neurotic angina pectoris was found in 11.5 per cent of cases, reflex angina in 4.7 per cent, the toxic form in 2.3 per cent and the anemic form in 2.8 per cent. The figures obtained for the incidence of the organic form agree strikingly with those obtained by some foreign authors. Gallavardin found organic forms in 78 per cent of his cases, White in 74 per cent and Lian in about 80 per cent. This comparison brought out that in at least three fourths or four fifths of cases angina pectoris has an organic substratum, cardiac infarction being present in every one of ten cases of organic angina pectoris. In 25.7 per cent of the cases of chronic organic angina a combination of the organic fundamental disease and functional factors was present. Coexisting functional factors were due to a reflex mechanism in 14.6 per cent of the cases of organic forms, to toxic influences in 7.1 per cent and to psychoneurotic agents in 4 per cent.

Angina pectoris begins most commonly in the fifth and sixth decades, and in the later decades the incidence decreases. This is in strong contrast to the age incidence of pathologic changes of the coronary vessels observed at necropsy, for these changes increase with the age of the subject. The authors then imply that an important cause of angina pectoris might be such agents as intense professional work and the irritations of everyday life, as well as sympathetic and endocrine disorders arising at the age of about 50.

Angina pectoris has a strong tendency to affect Jews, the incidence being nearly four times greater in Jews than in others. Women were affected in only 12.5 per cent of all cases. The majority of the subjects were well-to-do and intelligent.

Heredity is likely to play an important part in the genesis of angina pectoris: a history of cardiovascular diseases in parents or in kinsfolk was found in 41.6 per cent of all cases of angina.

Syphilis is held to be the cause in from a fourth to a fifth of all cases.

The role assumed by nicotine in producing angina pectoris has been overrated. Although there might be some individuals particularly sensitive to smoking, no parallel was found between the amount of smoking and the seriousness of the condition. The same is to be said concerning the influence of alcohol.

The duration of the disease from the onset of symptoms to the first consultation did not exceed five years in about 50 per cent of the cases. The average duration until the first consultation was from three to four years. According to the 140 replies to the inquiry, the average time of survival was eight years after the onset of the disease. Death occurred at the average age of about 64. It occurred most frequently within the first year of the disease; afterward the mortality rate decreased gradually until the ninth year, after which the chances for survival lessened.

In 83.1 per cent of cases the pain was located behind the sternum; most commonly it was felt transversely and in rare instances longitudinally. In 12.1 per cent of cases the pain was located far from the precordial region. The pain was accompanied by anxiety in 37.5 per cent.

The anginal attack could be provoked by physical efforts in 68 per cent of all cases, by emotional disturbances in 37 per cent and by heavy meals in 20 per cent.

Normal systolic arterial pressure was found in 31.9 per cent of cases. It was lowered in 17.1 per cent and elevated in 51 per cent. The average systolic pressure of all the cases of angina pectoris was 168.1 mm. In females this average systolic pressure was higher than in males: 183 against 166 mm. The average diastolic pressure was 99.1 mm. The authors emphasize the considerable difference between the average systolic and diastolic pressures.

As shown by an x-ray examination, structural changes in the aorta were present in 36 per cent of all cases. There was evidence of sclerosis of the peripheral arteries in about 60 per cent of the cases. Intermittent claudication coexisted in 2.8 per cent and it occurred most frequently in tobacco smokers.

Marriages

ARTHUR SUMNER BRINKLEY, Richmond, Va., to Miss Constance Elizabeth Brown of Greenwich, Conn., January 3.

WILLIAM EDWARD BARFIELD, Atlanta, Ga., to Miss Ellen Theresa Ryan of Savannah, Dec. 23, 1938.

WILLARD N. BLOME, Oak Park, Ill., to Miss Mabel Lillian Wingard of Chicago, February 11.

STEPHEN TRENT BARNETT JR., to Miss Josephine Meador, both of Atlanta, Ga., in February.

SAMUEL TAMARKIN to Mrs. Ida Broida, both of Youngstown, Ohio, recently.

Deaths

James Carroll Flippin ✠ Charlottesville, Va.; University of Virginia Department of Medicine, Charlottesville, 1901; member of the House of Delegates of the American Medical Association 1934-1938 and in 1936 was elected a member of the Council on Scientific Assembly for a term of five years to end in 1941; dean since 1924 and professor of internal medicine since 1915 at his alma mater, and at various times demonstrator of histology and pathology, adjunct professor of bacteriology and professor of clinical medicine; past president of the Medical Society of Virginia; aged 61; died, February 16, of heart disease.

William Gray Ricker ✠ St. Johnsbury, Vt.; Johns Hopkins University School of Medicine, Baltimore, 1904; member of the House of Delegates of the American Medical Association, 1925-1928, 1930, 1932-1934; past president and secretary of the Vermont State Medical Society; past president of the New England Medical Council; at one time chairman of the Vermont Department of Public Health; member of the American Academy of Ophthalmology and Oto-Laryngology and the New England Ophthalmological Society; aged 62; died, February 28.

Harry Philip Cahill ✠ Boston; Harvard University Medical School, Boston, 1911; assistant professor of otology at his alma mater and the graduate school; member of the American Academy of Ophthalmology and Oto-Laryngology, American Otological Society and the New England Otological and Laryngological Society; served during the World War; surgeon to the Massachusetts Charitable Eye and Ear Infirmary; aged 54; died, January 15, in the Peter Bent Brigham Hospital of cerebral hemorrhage, hypertension and cerebral thrombosis.

P. Maxwell Foshay ✠ New York; University of Pennsylvania Department of Medicine, Philadelphia, 1891; member of the House of Delegates of the American Medical Association, 1902-1903; vice president of the Mutual Life Insurance Company of New York; aged 71; died, January 26, at the Mountainside Hospital, Montclair, N. J., of coronary sclerosis and myocarditis.

Joseph Thomas Hornback, Nevada, Mo.; Kansas City Medical College, 1896; member of the Missouri State Medical Association; formerly secretary of the Vernon-Cedar Counties Medical Society; at various times county coroner, county health officer and treasurer of the school board; aged 66; died, Dec. 31, 1938, of cerebral hemorrhage.

Inman Williams Cooper ✠ Meridian, Miss.; University of Tennessee Medical Department, Nashville, 1903; past president of the Mississippi State Medical Association; served during the World War; formerly member of the state board of health; aged 56; died, January 26, at the Rush's Infirmary of cirrhosis of the liver.

Chester Dale Christie ✠ Cleveland; Western Reserve University School of Medicine, Cleveland, 1913; assistant clinical professor of medicine at his alma mater; served during the World War; aged 52; on the staff of the Lakeside Hospital, where he died, January 27, of coronary thrombosis.

Frank Guillemont ✠ Niagara Falls, N. Y.; Western University Faculty of Medicine, London, Ont., Canada, 1893; on the staff of the Niagara Falls Memorial Hospital; president of the board of managers, Niagara Sanatorium, Lockport; aged 66; died, Nov. 1, 1938, of coronary occlusion.

George Emmet Hart, Lyman, Neb.; Keokuk (Iowa) Medical College, College of Physicians and Surgeons, 1906; member of the Nebraska State Medical Association; aged 62; died, Nov. 6, 1938, in the West Nebraska Methodist Episcopal Hospital, Scottsbluff, of lobar pneumonia.

Arthur Thomas Paull, Flint, Mich.; Detroit College of Medicine, 1909; member of the Michigan State Medical Society; served during the World War; aged 61; died, Dec. 11, 1938, in the Women's Hospital of heart disease and pneumonia following influenza.

Justin E. Rowland, South Euclid, Ohio; Homeopathic Hospital College, Cleveland, 1891; past president of the county school board; aged 74; died, Dec. 9, 1938, in the Huron Road Hospital, East Cleveland, of coronary thrombosis.

Willis F. Huntsman ✠ Lexington, Tenn.; University of Tennessee Medical Department, Nashville, 1900; past president of the Henderson County Medical Society; aged 70; died, Dec. 22, 1938, of coronary occlusion.

Edward J. Higgins, Joliet, Ill.; Northwestern University Medical School, Chicago, 1901; member of the Illinois State Medical Society; city health officer; aged 67; died, Dec. 24, 1938, of coronary thrombosis.

Alfred Ephraim Reiter, Melcher, Iowa; State University of Iowa College of Medicine, Iowa City, 1901; member of the Iowa State Medical Society; aged 61; died, Dec. 8, 1938, of cardiorenal vascular disease.

David Wells Register, Columbia, S. C.; Atlanta Medical College, 1914; member of the Medical Association of Georgia; aged 52; was found dead, Dec. 22, 1938, of carbon monoxide poisoning, self administered.

James John Conlon ✠ Cuyahoga Falls, Ohio; University of Michigan Homeopathic Medical School, Ann Arbor, 1915; aged 54; died, Dec. 2, 1938, in the City Hospital of carcinoma of the stomach.

David H. Kogan, Philadelphia; Universität Bern Medizinische Fakultät, Switzerland, 1919; on the staff of the Mount Sinai Hospital; aged 49; died, Nov. 23, 1938, of cerebral hemorrhage.

Jordan Lally ✠ Long Island City, N. Y.; University of Vermont College of Medicine, Burlington, 1921; aged 45; died, Nov. 26, 1938, in the New York Hospital of heart disease.

George William Woodnick, Los Angeles; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1906; aged 62; died, Nov. 10, 1938.

Jones Riley McMillan, Cardington, Ohio; Cincinnati College of Medicine and Surgery, 1895; aged 88; died, Dec. 13, 1938, of arteriosclerosis and chronic interstitial nephritis.

John B. Keaggy, Pittsburgh; Jefferson Medical College of Philadelphia, 1875; member of the Medical Society of the State of Pennsylvania; aged 86; died, Nov. 6, 1938, of uremia.

Walter Emil Frank ✠ St. Louis; Washington University School of Medicine, St. Louis, 1910; aged 52; died, Dec. 2, 1938, in the Lutheran Hospital of carbuncle on the neck.

William Otwa Lee, Danville, Va.; University College of Medicine, Richmond, 1903; aged 59; died, Dec. 31, 1938, in the Memorial Hospital of cancer of the pancreas and liver.

John Edwin Dearden ✠ New York; University of the City of New York Medical Department, 1891; aged 75; died, Dec. 10, 1938, in the Misericordia Hospital of pneumonia.

Hubert Lewis Hollenbeck, Los Angeles; State University of Iowa College of Medicine, Iowa City, 1900; aged 62; died, Nov. 18, 1938, of tuberculous bronchopneumonia.

Ezekiel E. Gillilan, Columbus, Ohio; Kentucky School of Medicine, Louisville, 1893; aged 66; died, Dec. 28, 1938, in the White Cross Hospital, of heart disease.

Szabo Serge Kalman, Roseville, Calif.; Univerzita Komenského Fakulta Lekárska, Bratislava, 1921; aged 42; died, Nov. 21, 1938, of coronary occlusion.

William John Sweasey Powers, New York; Cooper Medical College, San Francisco, 1904; aged 63; died, Dec. 12, 1938, of acute dilatation of the heart.

John Bernhard Egts, Delphos, Ohio; Homeopathic Hospital College, Cleveland, 1885; formerly city health commissioner; aged 87; died, Nov. 5, 1938.

Franklin Charles Hull, Twining, Mich.; Saginaw Valley Medical College, Saginaw, Mich., 1901; aged 59; died, Dec. 9, 1938, of cerebral hemorrhage.

Wellford B. Lorraine, Richmond, Va.; Hahnemann Medical College and Hospital, Chicago, 1906; aged 58; died, Nov. 12, 1938, of cerebral hemorrhage.

John Robert Pate, Los Angeles; Central College of Physicians and Surgeons, Indianapolis, 1897; aged 71; died, Nov. 5, 1938, of coronary occlusion.

Charles Jeremie Coulombe, St. Justin, Que., Canada; Victoria University Medical Department, Coburg, Ont., 1872; aged 92; died, Dec. 1, 1938.

Robert E. La Rue ✠ Erie, Ill.; Louisville (Ky.) Medical College, 1894; aged 64; died suddenly, Dec. 6, 1938, of coronary sclerosis and myocarditis.

Robert A. Blackburn, Glendale, Calif.; Hahnemann Medical College and Hospital, Chicago, 1886; aged 82; died, Nov. 24, 1938, of acute nephritis.

William Randolph Pettit ✠ Brooklyn; Long Island College Hospital, Brooklyn, 1901; aged 66; died, Nov. 11, 1938, of cerebral hemorrhage.

Carl Huston Wright, Yorktown, Ind.; Medical College of Indiana, Indianapolis, 1903; aged 60; died, Nov. 25, 1938, of angina pectoris.

Harry Sutphin Hatch, Madison, Ind.; Pulte Medical College, Cincinnati, 1892; aged 71; died, Nov. 29, 1938, of cerebral hemorrhage.

Correspondence

THE CHEMIST IN THE MEDICAL LABORATORY

To the Editor:—The place of the chemist in a clinical laboratory cannot be evaluated either by a busy physician or by a chemist without experience in laboratories. The problems of each laboratory are different.

From personal experience I feel that the chemist undervalues the participation of the physician in his laboratory work and that few physicians quite understand the purpose of the chemist. The less participation on the part of the physician in the clinical laboratory, the better for the essential work of the laboratory. At the same time, the fewer times the chemist is called on for his opinion as to whether a given determination is normal or pathologic, the better for the patient and the hospital. A physician, who believed his knowledge of chemistry to be adequate and who was asked to pass critical judgment on the work of the laboratory studied the intricacies of the work, and his confidence lessened at every step. Modern clinical chemistry involves, or at least should involve, the frontier of chemistry. An active physician cannot possibly keep abreast of the rapid developments in practical chemistry. I should ask for no better proof of the inadequacy of the determinations of the laboratory than that the attending physician "knows" what is going on. The physician gains little from his exposure to chemistry at best. Much pseudochemistry is encountered by the student after he leaves the chemistry laboratory by overenthusiastic teachers of other subjects. The ideal, of course, is to have in charge of the laboratory a man who has received fundamental training in chemistry in his premedical years and then taken a medical degree, but these men are rarely available and, when available, are frequently undesirable for one reason or another. It is far better to adopt the scheme that has been found to work with unquestionable efficiency: Let the physician ask the laboratory for certain definite determinations. Let the laboratory make the determination as its experience and judgment dictate. Let the interpretations lie with the physician. It is he, not the chemist, who can maintain touch with the meanings of results, the normals and the departures. The chemist has his chore in keeping abreast of the chemical times. The chemist is apt to accept as normal not the data given by his own observations but those published from some distant, perhaps foreign, laboratory. A certain chemist pasted into the end boards of a book he had written a series of normals as he gained the data from reading but checked against his own results interpreted as normal by a medical colleague (applied Biochemistry, ed. 2, Philadelphia, W. B. Saunders Company, 1927), yet the list has been subjected to violent criticism, which is justified since the data applied more to the locality in which the determinations were made and less to the results of others in different regions. The physician should see that he is supplied by his laboratory with normals for the region in which he is working and draw conclusions of deviations from these normals as to whether his laboratory reports are within normal limits. Only the physician can determine whether the patient from whom the specimen is taken is normal or otherwise.

And so I would recommend the Monroe Doctrine for the clinical laboratory: The laboratory for the laboratory worker; interpretations for the physician. Far better than placing a medical man in charge of a laboratory is the procedure adopted by many fine institutions, namely, to have one or more chemists of unquestioned standing act as consultants to insure that the methods employed by the laboratory worker are acceptable and modern. Industries pay roundly for such services, but they reap rewards.

WITHROW MORSE, PH.D., Lake Bluff, Ill.

THE CLINICAL APPLICATION OF DUODENAL EXTRACT

To the Editor:—Since reporting on the clinical application of duodenal extract (Macallum-Laughton) in the treatment of diabetes (Duncan, G. G.; Shumway, N. P.; Williams, T. L., and Fetter, Ferdinand: *Am. J. M. Sc.* **189**:403 [March] 1935), my associates and I have received many inquiries regarding the action of this preparation and the likelihood of its permanent value, but most of all its availability for distribution. At least one pharmaceutic firm has quoted our work as corroborating their questionable observations. We of course were not consulted about having our names used for this purpose.

It seems appropriate to recount, through the medium of THE JOURNAL, our disappointments, difficulties and the present status of this problem.

Following the apparently excellent results with two or three batches of the extract, made up in small quantities, the effect was lost when treatment with material made in large lots was begun. The former insulin requirement of the two children (G. D. and A. B.) returned. The two patients (T. G. and R. M.) who had been admitted in ketosis were obliged to resume taking large amounts of insulin several weeks after the apparently effective batch of extract was exhausted in spite of the normal dextrose tolerance curves obtained while receiving the extract.

In the interim between 1935 and the present (January 1939) we have not been able to reproduce our original results either in the original or in new patients. It is true that mild beneficial effects were noted occasionally, but they were not maintained nor were they convincing when subjected to critical analysis.

Under the assumption that the original extract made in small batches was effective, the following possible causes for the loss in potency have been considered: (1) changes from small to large quantity production; La Barre's method of isolating the duodenal hormone which was clinically successful in laboratory preparations has also failed to give active material in mass production; (2) changes in the method of extraction and preservation, and (3) obtaining the extract from animals which had not been fed for several days before being slaughtered. This is the most probable. Macallum (*Canad. Chem. & Process Industries* **22**:13, 1938) indicates that there is active material, physiologically identical to Young's glycotrope but possessing greater stability, in the pancreas of starving cattle but that the problem of isolation is complicated by the presence of insulin and a powerful insulin antagonist.

After a survey of the clinical results, the following just criticism can be offered: New patients with diabetes were used for our observations and not patients who had had the disease for long periods and whose insulin need was thoroughly known.

There are rare diabetic patients who present an apparently severe form of diabetes when first seen but who, following initial treatment, do well on diet therapy alone for a short period but eventually need large amounts of insulin. That several of these patients should be seen consecutively, as would appear to be the case if this explained our results, is most unlikely, especially when two were children and one was an adolescent youth.

In summary, we have been unable to confirm our early results but believe that the striking effects obtained from an apparently potent duodenal extract were not merely coincidental. Clinical work with the extract has been discontinued pending the outcome of animal experimentation which is being actively pursued by Macallum.

GARFIELD G. DUNCAN, M.D., Philadelphia.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

CEMENT BURNS AND DERMATITIS

To the Editor:—1. What is the best treatment for skin burns from wet quick setting cement? 2. What is the incidence of recurrence of cutaneous eruptions at the sites of old cement burns? Is the development of blebs containing clear fluid on the once healed areas a criterion of chronic cement poisoning? 3. Is it possible that painful hip and knee joints could be caused by extensive cement burns on the legs three weeks after the wounds have healed?

M.D., Texas.

ANSWER.—1. Quick setting cements may contain, in addition to calcium oxide, such other cutaneous irritants as potassium sulfide, sodium carbonate, potassium carbonate, alum, calcium chloride and aluminum chloride, but the treatment for burns caused by quick setting cement is the same as for burns caused by ordinary cement, viz. the application of mild palliative lotions such as boric acid solution, calamine lotion or soothing ointments such as boric acid ointment, zinc oxide ointment or calamine ointment. In addition to this the worker should be removed from further exposure to the cement.

2. Cutaneous eruptions at the sites of old cement burns should not recur unless there is a fresh exposure to cement. However, workers with psoriasis or lichen planus may have an occurrence of these diseases on the site of old cement burns.

The development of blebs containing clear fluid on the once healed areas of cement burns is not a criterion of chronic cement poisoning. There is no such condition as a chronic cement poisoning in the same sense as there is a chronic lead or benzene poisoning. If a dermatitis caused by cement is not properly treated and the exposure to cement continues, a chronic eczema may result. In this condition the skin is thickened and may have cicatricial infiltrations which may become covered with vesicles and pustules. Conjunctivitis and ulcers of the mucous membranes of the nose and mouth and fever may develop at this stage. Such a condition might be termed by the workers chronic cement poisoning.

3. Extensive cement burns on the legs three weeks after the wounds have healed may cause painful hip and knee joints if the cicatrices are deep and pull on the joints, but workers with cement in the open air may suffer from rheumatic pains in the joints resulting from rapid changes in temperature, strain and fatigue, and not due to any damage caused by the cement.

Further information on cement dermatitis may be found in Queries and Minor Notes, THE JOURNAL, Nov. 12, 1938, page 1867.

PAPULAR URTICARIA AND ALLERGY

To the Editor:—Will you kindly advise me just what is the underlying cause or what are the factors involved in the well known fact that the urticaria of infants and young children is so frequently papular, vesicular or bullous, or a combination of such lesions, and that the lesions of urticaria in an adult are nearly always wheals. Is it a question of histopathologic differentiation or is it a matter of allergy? Kindly explain in detail, if possible.

ALBERT S. TENNEY, M.D., East Orange, N. J.

ANSWER.—First it must be emphasized that the adult type of urticaria (erythema with wheal formation) does occur in children. The type of urticaria which the inquirer describes as occurring in infants and young children no doubt has reference to lichen urticatus or urticaria papulosa. This urticarial manifestation appears to be common in Europe but less common in this country. The lesions begin with small areas of pale pink to deep red blotches or wheals. The wheals last for only a few hours and are frequently present only at night; therefore they are usually missed. The latter are replaced quickly by papules or vesicopapules. The papules last for several days or weeks. They are mainly above the surface of the skin. The itching often leads to excoriation and crusting and subsequent discoloration. Where the skin is thicker, large vesicles or bullae may result. The lesions are discrete and occur particularly on the extensor surfaces of the forearms and legs, on the buttocks and on the lower portion of the back.

The classic description of the tissue changes in the ordinary urticaria are those of capillary dilatation, areolar flush and wheal formation from increased permeability leading to localized edema. In lichen urticatus, Sequeira (Diseases of the Skin, New York, Macmillan Company, 1927) describes the papule as a papillary edema, with infiltration of leukocytes and dilatation of vessels. The corpus mucosum is edematous and under the stratum corneum there is a mass of imperfectly formed corneous cells. The cells of the epidermis are in a spongy condition, resembling that in eczema. While allergy is generally regarded as the most important single factor in the whealing type of urticaria, the status of allergy in papular urticaria is more uncertain and more complex. According to Bray (Recent Advances in Allergy, Philadelphia, P. Blakiston's Son & Co., 1934) in the majority of such cases dietary and thermal factors are involved. The dietary causes are due primarily to two types of foods. The fats, especially bacon and pork products and fish oil, constitute an important group. The other foods include common allergens such as egg, fish, potato and cocoa. In allergy to the first type of foods, cutaneous reactions are almost never obtained. The factor of heat is an important one, according to Bray, since this rash generally appears only in the warmer months or after warm baths, exercise or other causes for increased temperature of the skin.

It is quite evident, therefore, that lichen urticatus or papular urticaria shows evidence of histopathologic differentiation from the common urticarias. Whether this is due to the nature of the child's skin as differing from that of the adult's or whether the explanation lies in the difference of the etiologic factors cannot be definitely ascertained. Nevertheless, in the final analysis, the allergic background is usually present in both of these conditions.

TENDRA MEAT TENDERIZER

To the Editor:—A patient has inquired about "Tendra." It is used to brush on steak and is supposed to make the muscle tender, breaking down the fiber. The patient said it is made from a plant or fruit which comes from South America. Could this be harmful and should patients be advised against using it?

F. P. BENNETT, M.D., Alliance, Ohio.

ANSWER.—There are a number of "meat tenderizers" in addition to one marketed under the name of "Tendra" by Tendra Kitchens, Cincinnati. It appears from information available that Tendra (and some of the other preparations intended for "tenderizing" meat) is made from Carica papaya, or melon trees, of tropical and semitropical districts. The juice of the fruit contains a proteolytic enzyme called papain. Like trypsin, this enzyme is capable of digesting many proteins. From time to time such products have been introduced into therapeutics, although nowadays they have received little use in that connection. It is claimed that by applying an extract containing papain to tough meat it can be rendered more tender, probably by the partial digestion of some of the connective tissue. According to a report of Shiro Tashiro and L. H. Schmidt in the *American Journal of Physiology* (**119**:413 [June] 1937) the product is nontoxic when ingested in small amounts by mouth, but workers and others handling the material must exercise precautions to keep their hands washed because otherwise the papain will attack the skin. According to a release of the Federal Trade Commission, the Perfect Manufacturing Company, trading as Tendra Kitchens, Cincinnati, has stipulated that it will cease representing that by using "Tendra" every portion of the meat can be cut with a fork and one can serve the "tenderest meat in town" and that use of "Tendra" shortens the time of cooking by a definite percentage.

PEPTIC ULCER

To the Editor:—What is the consensus on the use of vitamins in duodenal ulcer and which vitamins seem most helpful? What are the latest books covering this? What books or other literature are available on other recent efforts in ulcer treatment?

GEORGE TAYLOR, M.D., Mooresville, N. C.

ANSWER.—Vitamins have no specific role in the treatment of duodenal ulcer. However, because of the fact that many of the diets for ulcer produce an avitaminosis it might be well to incorporate mixtures of vitamins in the therapy of peptic ulcer. Furthermore, because a patient may have had a previous limited intake of a sufficient number of vitamins, it might be included a priori in the diet at the beginning. The latest book on the treatment of ulcer is by G. B. Eusterman and D. C. Balfour (The Stomach and Duodenum, Philadelphia, W. B. Saunders Company, 1935). The following are the references for some of the newer works on peptic ulcer:

Metz, M. H., and Lackey, R. W.: Posterior Pituitary Extract, *Dallas M. J.* **24**: 46 (April) 1938.

Jones, C. R.: Colloidal Aluminum Hydroxide, *Am. J. Digest. Dis. & Nutrition* **4**: 99 (April) 1932.

Mutch, Nathan: Hydrated Magnesium Trisilicate, *Brit. M. J.* **1**: 254 (Feb. 8) 1936.

Emery, E. S., Jr., and Schnitker, M. A.: Effect of Administration of Bile, *Ann. Int. Med.* **11**: 2007 (May) 1938.

HAZARDS FROM GLUE MANUFACTURE

To the Editor:—I wonder whether there is any industrial hazard in the manufacture of an envelop glue which consists of a tapioca dextrose mixture and acetic acid, which is boiled together for about five hours. A patient says that he has headaches daily, which are increased by the fumes of this mixture. The reflexes, the Wassermann reaction and the heart are normal. Blood examination gives hemoglobin 96 per cent (Sahli), 4,000,000 red cells, differential normal, 10,000 white cells.

M.D., Illinois.

ANSWER.—The characteristic point of attack of acetic acid vapors is the conjunctiva. Action may also be exerted on the mucous membranes of the respiratory tract and thereafter on the skin. Unless some of these manifestations have appeared, it is most unlikely that acetic acid is any direct producer of the headaches mentioned in the query. The tapioca powder conceivably might lead to allergic manifestations, of which headache might be one. When tapioca is boiled over a long period with acetic acid, the chemical reaction that takes place probably leads to hydrolysis with the possible formation of polyhydroxy compounds. Higher aldehydes may be produced. However, it is not known that any of these compounds possess toxic properties. The presence of headaches under conditions of prolonged boiling of a product should lead to the suspicion of carbon monoxide poisoning, particularly if gas is the fuel.

STATURE OF AMERICANS

To the Editor:—Kindly give me the average height for the full grown normal American male and female of this present generation.

M.D., Ohio.

ANSWER.—This question was referred to Prof. E. A. Hooton of the Department of Anthropology of Harvard, who has kindly supplied us with the following tables:

Statures of Americans (Native Born of Native Parentage)

Males

	Age Range	Number	Stature Cm.	Stature Inches	
Century of Progress	15-84	1544	174.81	68.82	(geographic totals)
Criminals	15-79	4201	171.90	67.67	
Harvard sons	17-21	480	177.50	69.88	

Females

	Age Range	Number	Stature Cm.	Stature Inches	
Century of Progress	15-79	1840	162.03	63.79	(geographic totals)
Eastern college women	17-19	571	164.53	64.78	

INTRAVENOUS DEXTROSE AND BLOOD AGGLUTINATION

To the Editor:—It has been stated that at least four hours must elapse after a patient has had dextrose before the blood is suitable for cross matching with a donor's blood. The presence of 5 or 10 per cent dextrose in the blood stream is said to favor false agglutinations. Is this correct?

M.D., Idaho.

ANSWER.—The intravenous injection of 5 or 10 per cent dextrose solution does not give rise to false agglutination. While it is true that in vitro high concentrations (above 5 per cent) of dextrose can cause agglutination of red blood cells, in vivo such concentrations are never reached after intravenous injection. It is obvious that if intravenous injections of dextrose were to give rise to false agglutination, attention would have been called to this fact by individuals doing grouping tests, yet no report of such a phenomenon has been published in the literature.

HEPTYL ALDEHYDE AND MOUSE TUMORS

To the Editor:—I noticed the request from Dr. A. Gaebler in Queries and Minor Notes January 28 about heptyl aldehyde in mouse tumors. One reference to Dr. Strong's work is found in *Science* (87: 144 [Feb. 11] 1938). Dr. Frank Dickens in the 1938 report of the British Empire Cancer Campaign reports work that he has done with Dr. E. W. Miller with feeding heptaldehyde to tumor-bearing animals and also with injections of the substance dissolved in sesame oil. He states that neither in transplanted nor in spontaneous mouse tumors have any marked effects on the growth of the tumors been observed, although with the transplanted tumors there was slight retardation, but it was not possible to state at that time whether or not retardation was significant. He states further that the respiration of tumor tissue (Walker carcinoma and Jensen sarcoma) is more susceptible to heptaldehyde than is normal rat tissue (liver, kidney, testis) but that brain is also rather susceptible. No work on man is reported.

RALPH L. HOFFMAN, M.D., San Diego, Calif.

Council on Medical Education and Hospitals

ANNUAL CONGRESS ON MEDICAL EDUCATION AND LICENSURE

Thirty-Fifth Annual Meeting, held in Chicago, Feb. 13 and 14, 1939

DR. RAY LYMAN WILBUR, Stanford University, Calif., in the Chair

COUNCIL ON MEDICAL EDUCATION AND HOSPITALS

FEBRUARY 13—MORNING

Protection of the Public Through Activities of the Council on Medical Education and Hospitals

DR. RAY LYMAN WILBUR, Stanford University Calif.: Among the really great possessions of the human race are the code of ethics and other traditions of the medical profession. Rooted in the remote past and of steady growth over the centuries. the established relations of the physician to his patient and to the public have seemed so necessary that they have been taken largely for granted. To grasp their great values, one need think only of what would have happened if medicine had been operated on a cut-throat competitive basis regardless of anything else than the money involved. What a sinister picture it would be if the traditions of the profession based on long experience had not been a controlling factor at the beginning of this modern era of the application of science to the relief of human ills. The potentialities of the doctor for good or evil in private life, in organized society and in public health are great. It would be impossible to control him by fiat or legislative acts. There is no possible substitute for competence in medical care, and competence can come only from education and training. There is a constant increase in the number of people who want good medical care and who know its value. A great movement is stirring for a wider spread of such care throughout the country.

The work of the physician brings him imperative lessons on the damage done to human lives through ignorance. His constant battle with the quack is based on the results to human lives which he knows have come from improper or inadequate treatment fostered by false promises. A lack of scientific appreciation and training makes it difficult for the public to judge many medical questions. So few persons understand biology or know anything about life except that they are living that naturally many can be easily imposed on.

The physician has led in all civilized countries in the efforts to control the activities of those who are inadequately trained for the care of the sick. The public itself has no adequate way in which it can give protection to individuals or to the community without the intervention of the trained scientist and the expert physician.

The policy of licensing physicians was first started in the United States in New York in 1766. Since that time various methods have been employed in an effort to secure for the public an assurance of competence in the practice of medicine. Examining boards of various sorts have been set up. Limitations have been placed around membership in medical societies. Public officials have had to meet certain requirements and have been appointed or elected to carry out the provisions of health laws. Reciprocity between various states has been devised. A national examining board has been set up. These procedures, no matter how carefully conducted, fail to accomplish many of the results desired. Experience has shown that the only real safeguard which the public has is the requirement that candidates for medical licenses be graduates of established medical schools of good quality. In the past, large numbers of medical schools that gave a valueless education have been chartered by the state. When those associated with the American Medical Association decided that steps should be taken to insure a better training of physicians, the Council

on Medical Education was set up to provide those interested, including the state boards of registration, with a reliable and impartial list of medical schools worthy of recognition. No agency except the American Medical Association could be depended on to procure this information in an impartial manner and to present it to the public. The American Medical Association has broad enough shoulders to take the responsibility and can stand up for standards for the protection of the public even at the expense of certain schools. As a result of the activities of the Council on Medical Education, which later took on the responsibility of rating certain educational features of the hospitals as well, there has been an unparalleled advance in the last thirty years in medical education. The Council is without power over these medical institutions. It can only try to discover the facts, make them public and indicate its judgment as to the merits or demerits of the medical schools or the hospitals for the training of those who are to care for the sick. Its relationship to the hospitals depends on the internships for young physicians and graduate work. It aims to see that no young doctor wastes his time on an internship in which it is impossible to gain sufficient experience and that a physician seeking further training gets full value for his time. A record is maintained of every practitioner from the time he enters medical school until his death.

The activities of the American Medical Association through the Council on Medical Education and Hospitals constitute one of the most potent forces for the protection and care of the health of the American people. Only by learning continuously and keeping up to date can the physician render the best service. The Council therefore has interested itself in the instruction of graduate physicians in medical schools and hospitals and in the development of educational programs in the county, state and national medical societies. It has taken a part in the preparation of opportunities for specialists and in devising plans by which suitable recognition can be given to those who have had satisfactory training. Only trained physicians can judge just what a medical education should be or test the candidate for practice as to competence. The acceptance by the American Medical Association of this great task has resulted in a major service to all mankind.

College Education for the Future Doctor

JAMES B. CONANT, PH.D., Cambridge, Mass.: This paper will be published in full in THE JOURNAL.

Organization and Subject Matter of General Education

ROBERT MAYNARD HUTCHINS, LL.D., Chicago: This paper will be published in full in THE JOURNAL.

Canadian Experiments in Medical Economics

DR. T. C. ROUTLEY, Toronto, Ont.: This paper will be published in full in THE JOURANAL.

FEBRUARY 13—AFTERNOON

DR. CHARLES GORDON HEYD, New York, in the Chair

The South as Testing Ground for the Regional Approach to Public Health and Public Welfare

HOWARD W. ODUM, LL.D., Chapel Hill, N. C.: There are so many facts available that it seems best to present my comments in a sort of factorial syllabus in which a series of assumptions constitutes the premises for discussion:

1. Public health is a new problem arising from the extraordinary developments in the trends of population, in modern technologic civilization and from the increasingly vital relation between the economy of the people and the health of the people.

2. The population of the Southern states is being, and will continue for a long time to be, reproduced more rapidly than that of any other region of the nation. Its excess of births over deaths is 10 per thousand, as compared with the national average of 7 per thousand, and already it has the most thickly populated rural area in the United States. Of the 108,600,000 native-born persons in the country in 1930, 28,700,000 were born in the Southeast, all but 4,600,000 in rural districts. Since the turn of the century the South has sent into the rest of the nation something like 4 million people. It is clear how important to the nation the health and vitality of the southern people are.

3. The South is a region of multiple cultures, with subregions representing the lowest measure of health efficiency in the nation and other subregions approximating high standards. Considering the rural and frontier nature of the culture, the situation is often not half so alarming as it appears to the citizen and student versed only in the perfection of urban health and sanitation.

4. The southern regions reflect an extraordinary deficiency in nearly all aspects of public health and medical services and many special problems are found in the South on which special attack must be made for the good of the people, the region and the nation. It is possible to point out a nucleus of four counties in a state of the lower South which had a death rate in 1935 from malaria of from 116 to 130 per hundred thousand of population, as compared with only 21.6 for the whole state and 3.6 for the nation. This subregion is surrounded by five counties with a rate of from two to three times the rate of the state and from ten to twenty times the national rate. It is possible also to select a group of counties in the Piedmont subregion with an estimated incidence of 600 cases of pellagra per hundred thousand of population. In another state of the lower South the 1935 health indexes for the whole state indicate that more than three of every hundred people have actually been reported as having malaria, nearly two of every thousand as having pellagra and hookworm and about the same number as having social diseases. It is generally recognized that morbidity is greatly under reported.

One may follow this first series of assumptions with a second series, somewhat more specifically applied to the South:

1. A problem to be attacked is that of developing a more balanced economy, in which the income and wealth of the people of the South may approximate adequacy for higher standards of living and a richer culture. All the king's horses and all the king's men cannot put together the components which go into an adequate health and medical service for a majority of the people whose income is simply not adequate.

2. On the other hand, the great majority of southern rural folk cannot attain economic effectiveness until they have been adequately conditioned in health and vitality.

3. Basic both to the explanation of the health situation and to the planning of the future is the recognition that a first task, almost prior to public health and medical technic, is provision for adequate diet and general home regimen and sanitation. This applies particularly to pellagra and hookworm, on the one hand, and, on the other, to the importance of recent discoveries and contributions in the field of biochemistry and nutrition in the reconstruction of an entire group of people. The minimum dietary requirements for the whole Southeast may be set at 2,450,000,000 gallons of milk, of which there is a production deficit of 1,161,455,000 gallons. Only 62 per cent of all farms reported cows milked, and the average number of gallons per animal was only 394, as compared with 618 for the Northeast, 638 for the Far West and 530 for the Middle states. The number of pure-bred cattle per farm is less than 1 per cent, as compared with 28 per cent for the nation.

4. A prime problem, again almost preceding the problem of the technical tools and administration of public health and medicine, is general health education. It may be no reflection on the people but it is no alteration of the fact that, without opportunity to understand the fundamentals of health, medicine and hygiene, as well as the essential meaning of high standards of living, of work and of food values, the people do not understand needs, opportunities and fundamentals. Many not only do not understand but would oppose standards and procedures. They would continue in many of the folk beliefs and practices which have held them back. There must be an effective bar-

rage of school and adult education to pave the way for the public health program. Indeed this is a part of the testing field for realistic public health planning.

5. Another assumption with reference to the South as a testing field for public health and medical service is that the burdens and handicaps which come from present and prospective deficiencies fall extremely hard on the youth, who, like the youth of the rest of the nation, search for security and reality. In the present and prospective economy and culture of the region not more than half of the youth may hope, under the most optimistic of premises, to find either.

6. The last assumption in the second series has to do with the actual program of public health and medical services. The premise is that in the South there is a supreme need of immediately increasing programs of public health and medicine, accompanied by realistic programs of research, education and public welfare planning.

The third and last series of assumptions tends to focus more nearly on the implications of the other series in terms of programs:

1. There does not appear to be any alternative to an increasingly larger contribution to the problem on the part of public health agencies. Inherent in the assumption is the consideration that in proportion as the nation helps enrich its regions it enriches itself and prevents subsequent drain of its resources for relief.

2. In the regular normal machinery of the Southern states and in particular the county unit basis of their public services there is an admirable testing ground for wholesome and effective cooperation between and among the counties, the states and the federal government.

3. Success in all aspects must be predicated on the training and use of a larger number of public health officials and workers as well as the strengthening of the personnel and availability of medical and hospital services. Such training centers as are being developed in the Nashville-Vanderbilt region and in Southeastern Region 2, in the state of North Carolina, represent policies and procedures which should be strengthened.

4. There is an extraordinary need for more study and research in many areas. There are almost no reliable data to give an adequate basis for conclusions in relation to diet and climate in the South or with reference to the environmental influences in farm tenant and other groups.

5. In view of these facts and the fundamental situation with reference to the growing population and the inadequacy of resources, a fifth assumption naturally focuses on sound programs relating to birth control. The North Carolina birth control clinical services are representative of what might be done, clinics already being in operation in between sixty and seventy counties in the state.

6. There is great need for an increasing number of experimental services in this and in many other fields distributed throughout the various subregions and comprehending private and public efforts. The University of North Carolina Division of Public Health expects to have, through a grant from a private agency devoted to the study and reduction of social diseases, a full time professor of syphilology.

These assumptions indicate both the nature and the promise of the South as a testing ground for the regional approach to public health work. From the premise that the South has a superabundance of natural wealth and human wealth but that there is an extraordinary degree of waste in both, the conclusion is justified that for science, skill and the professions devoted to the development, conservation and utilization of all resources in harmony with a practical adaptation to the normal process of democratic government and civic cooperation it will constitute the perfect testing grounds for next steps.

DISCUSSION

DR. L. J. KOSMINSKY, Texarkana, Ark.: In Arkansas, under the state health officer, Dr. W. B. Grayson, there is a good strong program, with health units. The counties do not all have them, but through the American Legion and the Forty and Eight, cooperating with the state department of public health, serums of all types, diphtheria toxoid and vaccines are being issued and typhoid immunization and treatment for syphilis are being given free irrespective of whether the recipient is indigent, in an effort to eradicate the diseases concerned. In my county in the last year several children were given rabies serum, which was furnished by the state health department. They were also given antitetanus serum. Physicians should teach rural families how to have good health and to provide during the productive months for foodstuffs for the winter. Many families who have milk and make butter and sell it in town do not give their children any milk or butter.

DR. R. N. WHITFIELD, Jackson, Miss.: I will be glad if you will not think that the South is in such a bad situation as you might from the address you have just heard. A man from the University of North Carolina got his Ph.D. degree by coming to my office and getting one year's statistics on births and going back in two or three weeks with his thesis. He had proved that the birth rate is higher on some soils than it is on others. I did not find out what soil it is in Mississippi that produces a higher birth rate than any other, but I might guess that it is sandy soil, down where they have or have had the hookworm disease. There are some good things in the South. The work of the state board of health is free from politics in Mississippi, and I understand that this is not true in a great many states in the North and in the East. Visitors have come from all over the United States, Europe, Asia and South America to learn our methods. There are only two states in the Union with a Negro population of less than 10 per cent that have a lower death rate than the white people of Mississippi. It seems that the South is a testing ground right now. I guess that there are 100 WPA projects in Mississippi alone—sewing projects and every other kind of project. The country down there is a little poor financially, but it is doing fine.

DR. ANTON J. CARLSON, Chicago: I have seen mass insufficiencies in nutrition in many parts of the world. I am disturbed by the speaker's all inclusiveness, as if the physician, under the program of public health, is to be the savior of mankind. I think that we shall have to differentiate a little. The doctor is not a farmer. Part of the difficulty with nutrition in the South is of course the lack of diversified farming and the lack of distribution of foodstuffs from other parts of the country. It would be unfortunate to hook up all these things, all the ills in the South, with what a program of public health is ordinarily understood to be. The program is entirely too broad for the doctor. Soil conservation, diversified farming and education in the fundamentals of biology and nutrition must be carried on through other agencies, which already exist. The essential program of public health should not be obscured by this all-inclusiveness. I listened to a Negro sharecropper from the South and he prided himself on the fact that there is no shortage in the crop of children. One of the big educational needs is what the speaker mentioned, namely birth control. There should be no pride in mere numbers, regardless of the proportion of incompetents and unfortunates.

DR. HOWARD W. ODUM, Chapel Hill, N. C.: Because the problem is so important, so big and so conditioned by economic, social and historical factors, the physician cannot manage it alone; it must be a problem of cooperation. Few things are more futile than a superimposed artificial program, set up by a group of single-track specialists. Mississippi is my favorite state. I was three years at the university. The man mentioned took five years to get his doctor's degree, and he is teaching at the University of Florida. Southerners are the best people in the world, but I am looking at facts as they are, and they must be faced. I want to stress the nonacademic realistic, practical value of recognizing the regional folk, because in diversity there is strength in America.

(To be continued)

Medical Examinations and Licensure

COMING EXAMINATIONS

STATE AND TERRITORIAL BOARDS

ALABAMA: Montgomery, June 20-22. Sec., Dr. J. N. Baker, 517 Dexter Ave., Montgomery.

ARIZONA: *Basic Science.* Tucson, March 21. Sec., Dr. Robert L. Nugent, Science Hall, University of Arizona, Tucson. *Medical.* Phoenix, April 11-12. Sec., Dr. J. H. Patterson, 826 Security Bldg., Phoenix.

ARKANSAS: *Medical (Regular).* Little Rock, June 8-9. Sec., State Medical Board of the Arkansas Medical Society, Dr. L. J. Kosminsky, 317 State Line, Texarkana. *Medical (Eclectic).* Little Rock, June 8-9. Sec., Dr. Clarence H. Young, 1415 Main St., Little Rock.

CALIFORNIA: *Written examinations.* San Francisco, July 10-13, and Sacramento, Oct. 16-19. *Oral examinations* (required when reciprocity application is based on a state certificate or license issued ten or more years before filing application in California), San Francisco, March 22, Los Angeles, August 7, and San Francisco, Nov. 15. Sec., Dr. Charles B. Pinkham, 420 State Office Bldg., Sacramento.

COLORADO: Denver, April 5-7. Sec., Dr. Harvey W. Snyder, 831 Republic Bldg., Denver.

CONNECTICUT: *Medical. Endorsement.* Hartford, March 28. Sec., Dr. Thomas P. Murdock, 147 W. Main St., Meriden. *Basic Science.* New Haven, June 10. *Prerequisite to license examination.* Address State Board of Healing Arts, 1895 Yale Station, New Haven.

DELAWARE: Dover, July 11-13. Sec., Medical Council of Delaware, Dr. Joseph S. McDaniel, 229 S. State St., Dover.

DISTRICT OF COLUMBIA: *Basic Science.* Washington, June 26-27. *Medical.* Washington, July 10-11. Sec., Commission on Licensure, Dr. George C. Ruhland, 203 District Bldg., Washington.

FLORIDA: Jacksonville, June 19-20. Sec., Dr. William M. Rowlett, Box 786, Tampa.

GEORGIA: Atlanta, June. Joint-Sec., State Examining Boards, Mr. R. C. Coleman, 111 State Capitol, Atlanta.

HAWAII: Honolulu, April 10-13. Sec., Dr. James A. Morgan, 48 Young Bldg., Honolulu.

IDAHO: Boise, April 4-7. Address, Dir., Bureau of Occupational License, Rm. 355, State Capitol Bldg., Boise.

ILLINOIS: Chicago, April 11-13, June 20-22, and Oct. 17-19. Superintendent of Registration, Department of Registration and Education, Mr. Homer J. Byrd, Springfield.

INDIANA: Indianapolis, June 20-22. Sec., Board of Medical Registration and Examination, Dr. J. W. Bowers, 301 State House, Indianapolis.

IOWA: *Basic Science.* Des Moines, April 11. Dir., Division of Licensure and Registration, Mr. H. W. Grefe, State Department of Health, Capitol Bldg., Des Moines.

KANSAS: Kansas City, June 13-14. Sec., Board of Medical Registration and Examination, Dr. J. F. Hassig, 905 N. 7th St., Kansas City.

KENTUCKY: Louisville, June 7-9. Sec., State Board of Health, Dr. A. T. McCormack, 620 S. Third St., Louisville.

MARYLAND: *Medical (Regular).* Baltimore, June 20-23. Sec., Dr. John T. O'Mara, 1215 Cathedral St., Baltimore. *Medical (Homeopathic).* Baltimore, June 20-21. Sec., Dr. John A. Evans, 612 W. 40th St., Baltimore.

MICHIGAN: Ann Arbor and Detroit, June 14-16. Sec., Board of Registration in Medicine, Dr. J. Earl McIntyre, 100 W. Allegan St., Lansing.

MINNESOTA: *Basic Science.* Minneapolis, April 4-5. Sec., Dr. J. Charnley McKinley, 126 Millard Hall, University of Minnesota, Minneapolis. *Medical.* Minneapolis, April 18-20. Sec., Dr. Julian F. Du Bois, 350 St. Peter St., St. Paul.

MISSISSIPPI: Jackson, June. Asst. Sec., State Board of Health, Dr. R. N. Whitfield, Jackson.

MONTANA: Helena, April 4-5. Sec., Dr. S. A. Cooney, 216 Power Block, Helena.

NEBRASKA: *Basic Science.* Omaha, May 2-3. *Medical.* Omaha, June 8-9. Dir., Bureau of Examining Boards, Mrs. Clark Perkins, State House, Lincoln.

NEVADA: Carson City, May 1-3. Sec., Dr. John E. Worden, Capitol Bldg., Carson City.

NEW JERSEY: Trenton, June 20-21. Sec., Dr. Earl S. Hallinger, 28 W. State St., Trenton.

NEW MEXICO: Santa Fe, April 10-11. Sec., Dr. Le Grand Ward, 135 Sena Plaza, Santa Fe.

NEW YORK: Albany, Buffalo, New York, and Syracuse, June. Chief, Bureau of Professional Examinations, Mr. Herbert J. Hamilton, 315 Education Building, State Education Department, Albany.

NORTH CAROLINA: Raleigh, June 19. Sec., Dr. William D. James, The Hamlet Hospital, Hamlet.

NORTH DAKOTA: Grand Forks, July 5-8. Sec., Dr. G. M. Williamson, 4½ S. Third St., Grand Forks.

OKLAHOMA: *Basic Science.* Oklahoma City, May 15. Sec. of State, Hon. C. C. Childress, State Capitol, Oklahoma City. *Medical.* Oklahoma City, June 14. Sec., Dr. James D. Osborn, Jr., Frederick.

OREGON: *Basic Science.* Corvallis, July 8, and Portland, Oct. 28. Sec. State Board of Higher Education, Mr. Charles D. Byrne, University of Oregon, Eugene.

PENNSYLVANIA: Philadelphia and Pittsburgh, July. Sec., Board of Medical Education and Licensure, Dr. James A. Newpher, 400 Education Bldg., Harrisburg.

RHODE ISLAND: Providence, April 6-7. Chief, Division of Examiners, Mr. Robert D. Wholey, 366 State Office Bldg., Providence.

SOUTH CAROLINA: Columbia, June 27. Sec., Dr. A. Earle Boozer, 505 Saluda Ave., Columbia.

SOUTH DAKOTA: Rapid City, July 18-19. Director, Medical Licensure, Dr. G. J. Van Heuvelen, State Board of Health, Pierre.

TENNESSEE: Memphis, March 22-23. Sec., Dr. H. W. Qualls, 130 Madison Ave., Memphis.

TEXAS: June. Sec., Dr. T. J. Crowe, 918 Mercantile Bldg., Dallas.

VERMONT: Burlington, June 14-16. Sec., Board of Medical Registration, Dr. W. Scott Nay, Underhill.

VIRGINIA: Richmond, June 21-23. Sec., Dr. J. W. Preston, 30½ Franklin Road, Roanoke.

WISCONSIN: *Basic Science:* Madison, April 1. Sec., Prof. Robert N. Bauer, 3414 W. Wisconsin Ave., Milwaukee. *Medical.* Milwaukee, June 27-30. Sec., Dr. Henry J. Gramling, 2203 S. Layton Blvd., Milwaukee.

NATIONAL BOARD OF MEDICAL EXAMINERS SPECIAL BOARDS

Examinations of the National Board of Medical Examiners and Special Boards were published in THE JOURNAL, March 11, page 1012.

Alabama Reciprocity and Endorsement Report

Dr. J. N. Baker, secretary, Alabama State Board of Medical Examiners, reports nineteen physicians licensed by reciprocity and one physician licensed by endorsement from Aug. 12 through Dec. 23, 1938. The following schools were represented:

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
University of Arkansas School of Medicine		(1936)	Arkansas
Denver Homeopathic College		(1901)	Colorado
Emory University School of Medicine		(1936)	Georgia
University of Illinois College of Medicine		(1931)	Missouri
Tulane University of Louisiana School of Medicine		(1921)	Virginia, (1932) Minnesota, (1937) Louisiana
University of Michigan Medical School		(1924)	Michigan
Washington University School of Medicine		(1936)	Missouri
New York University College of Medicine		(1936)	New York
University of Buffalo School of Medicine		(1936)	Ohio
Ohio State University College of Medicine		(1933)	Ohio
University of Oklahoma School of Medicine		(1934)	Oklahoma
University of Tennessee College of Medicine		(1931), (1936) (1937)	Tennessee, Louisiana
Vanderbilt University School of Medicine		(1935, 2)	Tennessee
Medical College of Virginia		(1917)	Maryland

School	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
Harvard University Medical School		(1931)	N. B. M. Ex.

Book Notices

Essentials of Pathology. By Lawrence W. Smith, M.D., Professor of Pathology, Temple University School of Medicine, Philadelphia, and Edwin S. Gault, M.D., Associate Professor of Pathology, Temple University School of Medicine, Philadelphia. With a foreword by James Ewing, M.D., Memorial Hospital, New York City. Cloth. Price, $9. Pp. 886, with 679 illustrations. New York & London: D. Appleton-Century Company, Incorporated, 1938.

This presents an interesting excursion in pedagogic technic, involving as it does the use of the case history method for teaching, which, in the words of Ewing's introduction, is employed "to take the teaching of pathology out of the realm of abstract philosophy and make it an effective force in the professional equipment of the medical student." The textbook which Smith and Gault have so constructed will provide an excellent instrument to test the advantages of teaching from this point of view. That the case history method will have advantages must be obvious. There are inherent dramatic features which arouse interest; there is close integration with the clinic, and with this an early familiarity with clinical terms is established; there is recognition that in reality "pathology" and "disease" are not to be compressed into stereotyped categories; finally there lurks the possibility that pathology will be envisioned as a dynamic process rather than as a wholly anatomic and static one. All these possibilities, though not expressed in the preface, were no doubt in the minds of the authors. The case history method may, however, bring with it disadvantages which must be considered from the standpoint of the instructor in pathology. Let us visualize a student out on the street on a dark night suddenly confronted with the dim outlines of a vast building. Myriads of dark windows range toward the sky. No street signs are visible, no door is evident; the student pries open a window, climbs in, turns on a light and examines the contents of the room. From one room he enters the next and repeats the process ad infinitum until he has examined every room. As he finds much of interest in many of the rooms, the tour becomes fascinating. Most of us, however, prefer to approach a building in daylight, knowing the street and number, observing its relation to adjacent structures. If the building is of importance, we might wish to know something of the architect and builder and possibly examine the floor plans, so that we may have some sense of direction, once we have entered the structure.

In pathology as projected for the student in the Smith and Gault manner the mental approach must involve something of the nature that has been implied because there is no beginning and no growth; only the finished and completed frame work is to have validity; the rest is not of the "essentials" and therefore can be sacrificed to the exigencies of the world's fast pace. One may deny the expediency while granting the exigency. We frequently decry the narrowness of the modern specialist, mourn the scholar of the passing generation. We realize the inherent dangers of our cubicle system of instruction and now we are

to teach this basic medical science as though it were another specialty. If the student is to get a broad perspective anywhere in medicine he must get it in pathology, for today there certainly is little perspective even in medicine as taught in modern medical schools. There is another possible difficulty. General pathology as now fitted into the medical curriculum is usually taught in the second year. In the case history method much clinical detail is involved the significance of which cannot possibly be grasped by a sophomore student who has never had contact with a patient, who has never taken a history, who in many instances is still in the early stages of his knowledge of physiology. It is doubtful whether a sophomore student is prepared to evaluate, even if he has time to absorb, all the clinical features spread out before him. That he is in danger of seeing the trees and not the forest comes to mind when one reads the chapters on inflammation, after all the keystone of any course in pathology. Nowhere are the obvious questions of why and how ever approached. But if the student is not to be interested in the basic reactions of inflammation, if he is to slur over the chemical and physical alterations that are reflected in his histopathologic slide, of what use is it to him merely to pile up the unlimited variety of the inflammatory pictures which the microscope can reveal?

This textbook is an experiment in pedagogy; the advantages that have been suggested for this method may possibly far outweigh the objections that are listed—and they have been listed not in criticism of the work, which is excellent, but possibly of the method. The authors and the publishers have provided a first class teaching apparatus; whether the method will be superior to the old one is a question that can be determined only after proper trial. Certainly no pathologist would suggest that we have perfected a teaching technic that could remotely be considered approaching an ideal. The text itself offers a well balanced presentation of both general pathology and the special pathology of the various organ systems. About one fourth of the text is devoted to the various degenerations and inflammations, another fourth to tumors, and the remaining half to special pathology. The descriptive text leaves nothing to be desired; it is clear and concise, and special effort has been made to present the orthodox point of view; controversial subjects have been avoided. While this at times results in a somewhat colorless impression, it has decided advantages in a book which aims at brevity in presentation. Reviewers can always find fault in the treatment of selected topics, but the teacher of pathology will probably find little cause for dissent. The paper used is not highly enameled, which makes for restful reading though it may possibly at times impair the quality of some of the illustrations. These are abundant and all are provided with concise and proper legends to integrate them with the text. They are by no means limited to the microscopic field but include also the gross specimen and in some instances the patient. In a series of color plates, drawings of microscopic fields have been reproduced; these include cells from inflammatory exudate, blood cells and arterial changes.

Chemie und Technik der Gegenwart. Herausgegeben von Dr. H. Carlsohn, Dozent an der Universität Leipzig. Band XV: Vitamine und Hormone und ihre technische Darstellung. Teil 1: Ergebnisse der Vitamin- und Hormonforschung. Von Dr. Hellmut Bredereck, Dozent an der Universität Leipzig, und Dr. Robert Mittag. Second edition. Boards. Price, 7 marks. Pp. 138. Leipzig: S. Hirzel, 1938.

This is a technical review of recent chemical research on the vitamins and hormones and is the first volume of a series. The remaining three volumes will be concerned with the preparation of vitamin and hormone products. The sex hormones will be the subject of a separate volume, the fourth in the series.

It is interesting to note that the authors refer to vitamin A as "axerophtol." This name is unfortunate because it refers to but one symptom of A deficiency in animals. Moreover, the name is chemically uninformative. The discussion of the chemistry of vitamin A is brief and clear. There is included a description of the synthesis of vitamin A according to Kuhn. Vitamin B_1, for which the authors have not used the preferred American term thiamin chloride, is also discussed briefly but in sufficient detail. The methods of preparation of riboflavin are described. Mention is made of some of the other members of the vitamin B complex, but no reference is made to nicotinic acid. Discussion of the organic chemistry of vitamin C is fairly complete. There is a brief description of vitamins D and E, with many chemical formulas. Brief mention is also made of vitamins H, J, K and P. There is a section also on the relation between vitamins and ferments which is limited to a discussion of the yellow ferment cocarboxylase and ascorbic acid. The organic chemistry of the hormones accounts for the subject matter of a little more than half of the book. A goodly portion of this material is concerned with sex hormones. There is a discussion of insulin, including the recent work on its composition. Epinephrine and the cortical hormone are discussed in detail. The chemistry of thyroxine is discussed briefly but adequately. Brief mention is made of the chemistry of the parathyroid, the hypophysis and other ductless glands, and to histamine, acetylcholine and related compounds. There is practically no mention of the hormones of the intestinal tract. This is surprising in view of the brief discussion of plant hormones with which the book concludes.

Emotion and the Educative Process: A Report of the Committee on the Relation of Emotion to the Educative Process. By Daniel Alfred Prescott, Ed.D., Chairman, Professor of Education, Rutgers University, New Brunswick, N. J. Cloth. Price, $1.50. Pp. 323. Washington, D. C.: American Council on Education, 1938.

This work is a report to the American Council on Education by the Committee on the Relation of Emotion to the Educative Process. It is a thoroughgoing report which analyzes the mechanisms of emotion and their application to teaching. The literature has been combed, and the material evaluated. In the introduction the author of the volume gives credit to other members of his committee for supplying most of the material; nevertheless he has compiled and written it, and he assumes the chief responsibility for the work. There are twelve chapters. The first four deal with psychologic descriptions of emotion and affective phenomena with the physiologic basis of emotion and behavior; one is devoted to a discussion of how greatly emotion may be modified by training. The book then passes on through the next several chapters to discuss what is meant by maturity and emotional reaction and how the basic personality needs are modified by various conditions so that maturity might not be arrived at; and there are discussions of the effects of contemporary social institutions on emotion. The remainder of the book treats of the influence of emotion on learning and evaluates the importance of education in controlling and modifying emotion. There are a number of individual discussions in these chapters which are of great value, not the least of which are incorporated in the eleventh chapter, dealing with personnel problems in education. In this chapter the question is brought up whether the educational profession satisfies the personality needs of teachers and points out how important maladjusted teachers are in disorganizing a school system. There are also discussions of the pupil-teacher relationship and how to deal with emotional problems in the school. The last chapter is a summary of the whole project. There is an excellent bibliography covering 180 references dealing with emotion and teaching. The whole work is a serious, comprehensive and worthwhile monograph. There are no case histories. The material is not particularly predicated for the medical man, but the psychiatrist, particularly the one who deals with children, should find the book of considerable interest in outlining the present status of emotion in terms of the psychology of learning and of education.

Guiding Human Misfits: A Practical Application of Individual Psychology. By Alexandra Adler, M.D., Research Fellow in Neurology, Harvard University. Cloth. Price, $1.75. Pp. 88. New York: Macmillan Company, 1938.

This little book is written by Alfred Adler's daughter. In a brief fashion Dr. Alexandra Adler attempts to cover the field of child guidance, neurosis in childhood, problems of adolescence, significance of dreams and earliest recollections, and some practical aspects of child guidance and psychotherapy; but since the book is not very extensive it is obvious that this must be carried out in a superficial fashion. Alexandra Adler's underlying psychiatric philosophy is that of her father, with some modification; namely, that people who are in an inferior position in life as the result of organic defect, rank in the family or social inferiority compensate for this and either retreat from reality through neurosis or into bad behavior. She cites numerous examples, not in the form of complete case histories but rather

in interesting but superficial discussion of many cases. Each chapter describes one or two illustrative cases but, of course, the whole field of behavior disturbance or neurosis is not covered. The author's experience with children seems to be limited by the fact that her philosophy of treatment is confined chiefly to the so-called individual psychology school of mental treatment. While there is no frank criticism of other schools of psychiatric thought, her vision is so limited that modern psychiatrists will not find that this book gives either a new and useful point of view or even a complete understanding of the mechanisms of behavior problems in children or of their treatment.

Alkoholæmi: Studier over Rusen. I. Af Max Schmidt. [Alcoholemia: Studies on Intoxication.] Denne Afhandling er af det lægevidenskabelige Fakultet antaget til offentligt at forsvares for den medicinske Doktorgrad, København. Paper. Pp. 328, with 20 illustrations. Copenhagen: NYT Nordisk Forlag, Arnold Busck, 1937.

This monograph is of great interest to physiologists, pharmacologists and physicians concerned with the medicolegal aspect of alcoholism. The author presents his own extensive studies of alcohol concentration in arterial, venous and capillary blood, in cerebrospinal fluid and in urine during the first two hours after taking various quantities of alcohol, on the fasting stomach and after food, and gives good critical summaries and evaluations of the relevant literature. The author's material includes also 400 medicolegal cases in which the amount of the alcohol ingested was unknown or in dispute. In the few cases tested the concentration of alcohol in the cerebrospinal fluid tended to exceed that in the arterial blood. The author studied also alcohol concentration in the blood of normal people not ingesting alcohol and accepts as probable the view that a trace of alcohol (production and ultimate oxidation) is part of normal metabolism and not dependent on fermentation of carbohydrates in the alimentary tract.

Medicine in the Outpatient Department: An Introductory Handbook. By Winthrop Wetherbee, Jr., M.D., Junior Visiting Physician, Boston City Hospital, Boston. With a foreword by George R. Minot, M.D., S.D., F.R.C.P., Professor of Medicine, Harvard University, Boston. Fabrikoid. Price, $1. Pp. 111. New York & London: Paul B. Hoeber, Inc., 1938.

This excellent, simple book may be read with a great deal of pleasure and profit in about an hour. The author has collected many common experiences and routine procedures of medical practice which will help the student in his clinical study of the patient. Especially commendable is the collection of clinical maxims. Every student will appreciate these as his medical experience increases and every medical practitioner likewise will enjoy rereading them. This book supplies the long needed, practical suggestions so definitely lacking in the textbooks of physical diagnosis. It is a notable contribution.

Milk and Nutrition: New Experiments Reported to the Milk Nutrition Committee. Part III: The Effect of Commercial Pasteurization on the Nutritive Value of Milk as Determined by Experiments on Calves. From the National Institute for Research in Dairying (University of Reading) and the Rowett Research Institute, Bucksburn, Aberdeen. Paper. Price, 2s. Pp. 27. Shinfield, Reading, England: National Institute for Research in Dairying, 1938.

This report of the Milk Nutrition Committee is concerned with the Aberdeen studies of the relative effects of pasteurized and raw milk in the feeding of calves. An earlier report of this comprehensive investigation on the nutritive value of milk was concerned with the relative effects of pasteurized or raw milk on the growth and health of school children. As in the feeding experiments with children, so in the present better controlled experiments with calves there was little difference observed in growth on pasteurized as compared with raw milk. Because of the safety of pasteurized milk, the conclusion may be drawn that the pasteurization of milk is a desirable procedure in the preparation of milk for human consumption.

Text-Book of Histology for Medical Students. By Evelyn E. Hewer, D.Sc. Cloth. Price, $4.50. Pp. 365, with 340 illustrations. St. Louis: C. V. Mosby Company, 1938.

This is a concise, elementary textbook of histology written primarily for medical students. The text is generously illustrated with mediocre free hand drawings and photomicrographs. This publication lacks the fundamental detail necessary for understanding histology. It is far below the standard of textbooks of histology published in this country.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Evidence: Admissibility of Statements Made by Examinee to Examining Physician.—A physician, said the Supreme Court of Missouri, Division No. 2, who has been in attendance on a patient for the purpose of treatment, may testify as to present symptoms or complaints of his patient as told to him by his patient and also as to his observations from his examination of the patient. He may not testify, however, as to statements made by his patient with respect to his past physical condition or with respect to the circumstances surrounding the injury or the manner in which the injury was received. If, as was stated in the case of *Coghill* v. *Quincy, O. & K. C. Ry. Co.* (Mo.), 206 S. W. 912, the physician has examined a person for the purpose of preparing himself as a witness in a case then pending or which is expected to arise, different considerations must be recognized, for then there exists a temptation to falsify, or at least magnify, the true condition.—*Evans v. Missouri Pac. R. Co. (Mo.), 116 S. W. (2d) 8.*

Workmen's Compensation Acts: Insurer May Recover Damages from Physician Who Negligently Treats Employee.—Baker, in the course of his employment, injured his left leg and was treated by the company physician. A diagnosis of dislocation of the hip was made and treatment rendered accordingly. The patient, however, continued to complain of pain. About eight months after the injury, the physician discovered that "the man had really suffered a fracture of the bone at the neck of the femur, but thought he could see evidence of callous and 'thought probably he would get a fairly serviceable fibrous union.'" No change in treatment was prescribed. Pain in the leg persisted, there was some looseness at the left hip joint and the left leg was shorter than the right. Later the industrial commission sent the workman to another physician, who performed a reconstruction operation during which an ununited fracture at the neck of the femur was found with almost complete absorption at the neck and a small devitalized shell representing the head of the femur. While the workman thereafter gradually improved, he was permanently partially disabled.

Compensation was paid Baker and all his medical and hospital bills were paid. Subsequently he brought suit for malpractice against the company physician. The industrial commission, being the administrator of the state insurance fund from which compensation had been paid to Baker, intervened, alleging that Baker's cause of action had by statute been assigned to it and that it was subrogated to his rights. The trial court denied the right of the workman to recover from the physician but rendered judgment in favor of the industrial commission in an amount in excess of what it had paid. Pending an appeal to the Supreme Court of Utah the physician died, and his administrator continued the action.

The workmen's compensation act of Utah contains this provision:

> When any injury for which compensation is payable under this title shall have been caused by the wrongful act of a third person, the injured employee or in case of death his dependents, may at their option claim compensation under this title or have their action for damages against such third person; and, if compensation is claimed and awarded, the employer or insurance carrier having paid the compensation shall be subrogated to the rights of such employee or his dependents to recover against such third person; provided, if such recovery shall be in excess of the amount of the compensation awarded and paid, then such excess, less the reasonable expenses of the action, shall be paid to the employee or his dependents.

Under this provision, said the court, the industrial commission had the right to sue the company physician, for when Baker accepted compensation from the commission after he was aware of the negligence of the physician any right of action he had against the physician passed to the industrial commission. The trial court was warranted in finding, the Supreme Court thought, that the company physician in his

diagnosis and treatment did not exercise such reasonable care and diligence as is ordinarily exercised by physicians in the locality in which he practiced. Nor did the trial court err in admitting the testimony of physician witnesses as to what diagnosis in their opinion would have been made by the average practitioner in the community, having the roentgenograms before him and having had them taken under his orders or direction. The witnesses did not thereby pass on the question of negligence and thus invade the province of the jury. It is permissible, the court said, to allow a medical witness to testify as to what an ordinary physician in the locality holding himself out as able to interpret roentgenograms, could or should have seen in them.

Neither did the trial court err in rendering judgment for the industrial commission in a sum greater than the commission had paid out, the excess being payable to the injured workman. The workmen's compensation act clearly provides that a judgment against the third person tort-feasor may be recovered in excess of compensation awarded and paid but that excess must be paid to the workman.

For the reasons stated, the judgment in favor of the industrial commission against the physician was affirmed.—*Baker v. Wycoff (Utah), 79 P. (2d) 77.*

Society Proceedings

COMING MEETINGS

American Medical Association, St. Louis, May 15-19. Dr. Olin West, 535 North Dearborn St., Chicago, Secretary.

Alabama, Medical Association of the State of, Montgomery, April 18-20. Dr. D. L. Cannon, 519 Dexter Ave., Montgomery, Secretary.

American Academy of Tuberculosis Physicians, St. Louis, May 13-14. Dr. Arnold Minnig, 638 Metropolitan Bldg., Denver, Secretary.

American Association for the Study of Neoplastic Diseases, Detroit, April 6-8. Dr. Eugene R. Whitmore, 2139 Wyoming Avenue N. W., Washington, D. C., Secretary.

American Association for Traumatic Surgery, Hot Springs, Va., May 8-9. Dr. Ralph G. Carothers, 409 Broadway, Cincinnati, Secretary.

American Association of Anatomists, Boston, Apr. 6-8. Dr. E. R. Clark, University of Pennsylvania School of Medicine, Philadelphia, Secretary.

American Association of Pathologists and Bacteriologists, Richmond, Va., Apr. 6-7. Dr. Howard T. Karsner, 2085 Adelbert Rd., Cleveland, Secretary.

American Association of the History of Medicine, Atlantic City, N. J., April 30-May 1. Dr. Henry E. Sigerist, 1900 Monument St., Baltimore, Secretary.

American Association on Mental Deficiency, Chicago, May 3-6. Dr. E. Arthur Whitney, Washington Road, Elwyn, Pa., Secretary.

American College of Physicians, New Orleans, March 27-31. Mr. E. R. Loveland, 4200 Pine St., Philadelphia, Executive Secretary.

American Gastro-Enterological Association, Atlantic City, N. J., May 1-2. Dr. Russell S. Boles, 1901 Walnut St., Philadelphia, Secretary.

American Laryngological, Rhinological and Otological Society, Chicago, May 10-11. Dr. C. Stewart Nash, 277 Alexander St., Rochester, N. Y., Secretary.

American Medico-Legal Association, Chicago, May 12-13. Dr. Michel Pijoan, 124 Commonwealth Ave., Boston, Secretary.

American Pediatric Society, Sky Top, Pa., Apr. 27-29. Dr. Hugh McCulloch, 325 North Euclid Ave., St. Louis, Secretary.

American Physiological Society, Toronto, Canada, Apr. 26-29. Dr. A. C. Ivy, 303 East Chicago Ave., Chicago, Secretary.

American Psychiatric Association, Chicago, May 8-12. Dr. Arthur H. Ruggles, Butler Hospital, Providence, R. I., Secretary.

American Society for Clinical Investigation, Atlantic City, N. J., May 1. Dr. Isaac Starr, University of Pennsylvania Hospital, Philadelphia, Secretary.

American Society for Experimental Pathology, Toronto, Canada, April 26-29. Dr. Paul R. Cannon, Dept. of Pathology, University of Chicago, Chicago, Secretary.

American Society for Pharmacology and Experimental Therapeutics, Toronto, Canada, Apr. 26-29. Dr. G. Philip Grabfield, 319 Longwood Ave., Boston, Secretary.

American Society of Anesthetists, New York, Apr. 14. Dr. Paul M. Wood, 131 Riverside Drive, New York, Secretary.

American Society of Biological Chemists, Toronto, Canada, Apr. 26-29. Dr. C. G. King, Univ. of Pittsburgh, Dept. of Chemistry, Pittsburgh, Secretary.

American Society of Clinical Pathologists, St. Louis, May 12-14. Dr. Alfred S. Giordano, 531 N. Main St., South Bend, Ind., Secretary.

American Surgical Association, Hot Springs, Va., May 11-13. Dr. Charles G. Mixter, 319 Longwood Ave., Boston, Secretary.

American Therapeutic Society, St. Louis, May 12-13. Dr. Joseph F. Elward, 1726 Eye St. N.W., Washington, D. C., Secretary.

Arizona State Medical Association, Phoenix, Apr. 13-15. Dr. D. F. Harbridge, 15 East Monroe St., Phoenix, Secretary.

Arkansas Medical Society, Hot Springs National Park, May 8-10. Dr. W. R. Brooksher, 602 Garrison Ave., Fort Smith, Secretary.

Associated Anesthetists of the United States and Canada, St. Louis, May 15. Dr. F. H. McMechan, 318 Hotel Westlake, Rocky River, Ohio, Secretary General.

Association for the Study of Internal Secretions, St. Louis, May 13-14. Dr. E. Kost Shelton, 921 Westwood Blvd., Los Angeles, Secretary.

Association of American Physicians, Atlantic City, N. J., May 2-3. Dr. Hugh J. Morgan, Vanderbilt University Hospital, Nashville, Tenn., Secretary.

Association of Military Surgeons of the United States, Washington, D. C., May 8-10. Dr. H. L. Gilchrist, Army Medical Museum, Washington, D. C., Secretary.

California Medical Association, Del Monte, May 1-4. Dr. George H. Kress, 450 Sutter St., San Francisco, Secretary.

District of Columbia, Medical Society of the, Washington, May 3-4. Mr. Theodore Wiprud, 1718 M St. N.W., Washington, Executive Secretary.

Federation of American Societies for Experimental Biology, Toronto, Canada, Apr. 26-29. Dr. D. R. Hooker, 19 West Chase St., Baltimore, Secretary.

Florida Medical Association, Daytona Beach, May 1-3. Dr. Shaler Richardson, 111 W. Adams St., Jacksonville, Secretary.

Georgia, Medical Association of, Atlanta, Apr. 25-28. Dr. Edgar D. Shanks, 478 Peachtree St. N. E., Atlanta, Secretary.

Illinois State Medical Society, Rockford, May 2-4. Dr. H. M. Camp, 224 S. Main St., Monmouth, Secretary.

Iowa State Medical Society, Des Moines, Apr. 25-27. Dr. Robert L. Parker, 3510 Sixth Ave., Des Moines, Secretary.

Kansas Medical Society, Topeka, May 1-4. Mr. C. G. Munns, 112 W. 6th St., Topeka, Executive Secretary.

Louisiana State Medical Society, Alexandria, Apr. 24-26. Dr. P. T. Talbot, 1430 Tulane Ave., New Orleans, Secretary.

Maryland, Medical and Chirurgical Faculty of, Baltimore, Apr. 25-26. Dr. Walter Dent Wise, 1211 Cathedral St., Baltimore, Secretary.

Mississippi State Medical Association, Gulfport, May 9-11. Dr. T. M. Dye, McWilliams Bldg., Clarksdale, Secretary.

Missouri State Medical Association, Excelsior Springs, Apr. 10-12. Dr. E. J. Goodwin, 634 North Grand Blvd., St. Louis, Secretary.

Nebraska State Medical Association, Grand Island, May 2-4. Dr. R. B. Adams, 414 Federal Securities Bldg., Lincoln, Secretary.

New Mexico Medical Society, Gallup, May 11-13. Dr. L. B. Cohenour, 219 W. Central Ave., Albuquerque, Secretary.

New York, Medical Society of the State of, Syracuse, April 24-27. Dr. Peter Irving, 2 East 103d St., New York, Secretary.

North Carolina, Medical Society of the State of, Cruise to Bermuda, May 9-14. Dr. T. W. M. Long, Roanoke Rapids, Secretary.

North Dakota State Medical Association, Fargo, May 8-10. Dr. Albert W. Skelsey, 20½ Broadway, Fargo, Secretary.

Ohio State Medical Association, Toledo, May 3-4. Mr. C. S. Nelson, 79 E. State St., Columbus, Executive Secretary.

Oklahoma State Medical Association, Oklahoma City, May 1-3. Dr. L. S. Willour, Third and Seminole, McAlester, Secretary.

Pacific Coast Surgical Association, San Francisco, Oakland, Del Monte, March 28-31. Dr. H. Glenn Bell, University of California Hospital, San Francisco, Secretary.

Society for the Study of Asthma and Allied Conditions, Atlantic City, N. J., Apr. 29. Dr. W. C. Spain, 116 E. 53d St., New York, Secretary.

South Dakota State Medical Association, Aberdeen, Apr. 24-26. Dr. Clarence E. Sherwood, Madison, Secretary.

Tennessee State Medical Association, Jackson, Apr. 11-13. Dr. H. H. Shoulders, 706 Church St., Nashville, Secretary.

Texas, State Medical Association of, San Antonio, May 8-11. Dr. Holman Taylor, 1404 West El Paso St., Fort Worth, Secretary.

CENTRAL SOCIETY FOR CLINICAL RESEARCH

Eleventh Annual Meeting, Held in Chicago, Nov. 4 and 5, 1938

The President, DR. WILLIAM H. BUNN, Youngstown, Ohio, in the Chair

(Continued from page 1017)

Serum Sickness: Effective Treatment and Probable Prophylaxis by Means of Histaminase

DRS. LEE FOSHAY, Cincinnati, and O. E. HAGEBUSCH, St. Louis: The important work presented to the society last year by Dr. Grace Roth on histaminase indicated to us that this enzyme should be effective in controlling the symptoms and other manifestations of serum sickness. This expectation has been tested and verified by the treatment of twenty patients, selected at random, most of them with the severer forms of this disorder. Sixteen were treated on either the first or the second day of illness, and thirteen obtained relief in from eighteen to thirty-six hours or less. In most cases the clinical responses were actually dramatic. A beginning attempt at prophylaxis has been made, with extremely hopeful outlook. The treatment seems to be rational, highly effective, safe and devoid of untoward by-effects or after-effects.

DISCUSSION

DR. LOUIS E. PRICKMAN, Rochester, Minn.: I have not used this preparation in the treatment of serum sickness but I have had considerable experience with it in the treatment of vasomotor rhinitis. The study of vasomotor rhinitis has one outstanding advantage: it permits one to observe objectively changes which may occur from time to time. Of twenty-six carefully selected and studied cases of vasomotor rhinitis definite relief from this preparation was obtained in only nine (34 per cent). In four cases the results were questionable; in the remaining thirteen cases (50 per cent) no relief whatever occurred. On the other hand, striking beneficial results were obtained in certain cases in which my associates and I had tried many different means of relieving the distress without any benefit whatever. Although

certain of my patients have obtained satisfactory results from the use of this preparation, the results in the whole group of cases of vasomotor rhinitis are certainly in contrast to those reported by Drs. Foshay and Roth. This discrepancy may be attributable to many factors, only a few of which I shall mention. Vasomotor rhinitis is a chronic disease, in contrast to serum sickness, in which the symptoms are acute and not of long duration. One important point is the apparent variability of the material itself. This must certainly be reflected in the results reported, as it has been demonstrated both clinically and experimentally. Although the material is said to be nontoxic, and although Dr. Foshay has noticed no toxic effects in any of his cases, I have some evidence that there may be a limit of tolerance to the oral administration of the preparation. One of my patients who obtained great relief of vasomotor rhinitis (due to food sensitivity) from this material noted that when the dose was increased beyond a certain point she had distressing abdominal cramps. She is still using the material but must be careful not to exceed a certain dose. Finally, when the material is found to be effective in vasomotor rhinitis its use must be continued; it therefore does not appear to be a "desensitizing agent." It does not seem to affect the fundamental allergic nature of the patient but seems to have an effect on the allergic reaction.

DR. GRACE ROTH, Rochester, Minn.: I continue to obtain good results in patients who have a hypersensitivity to cold. I have added to that group some patients who are hypersensitive to insulin, with whom I am doing equally well. I want to call attention to the batches of the preparation sent out. The last patient with local hypersensitivity to insulin was put on one batch, and the local lesions disappeared. Then for two days I gave him tablets of another batch, and the local lesions returned; when I returned him to the tablets of the first batch the lesions disappeared, and he has had no further trouble.

DR. HEINRICH NECHELES, Chicago: I should like to ask the authors whether my impression was correct that histaminase given intramuscularly had a longer latent period than that given by mouth. It is known from the work of Best and his co-workers that the body contains much histaminase and the dose of a few units of histaminase administered by the authors seems to be therefore insignificant in comparison to what the body actually contains. Taking into consideration what Drs. Roth and Foshay said, I wonder whether the therapeutic effects reported may not be nonspecific rather than due to histaminase.

DR. PHILIP W. BROWN, Rochester, Minn.: I should like to ask the authors, for scientific as well as personal reasons, whether they have had opportunity to use this treatment for giant urticaria, or whether the rest of the discussers have had opportunity to use it.

DR. LEE FOSHAY, Cincinnati: I realize that we know little about the composition of this compound. It is undoubtedly a mixed substance, and how much of it is actually histaminase has never been shown. I think one should be careful about the selection of proper patients for its use. I am sure it is going to be widely used and abused for a great variety of demonstrated and suspected so-called allergies. I have heard from two discussers today and from other persons that different batches of the material have varied in potency. As I have said, all of mine came from one batch. The effect of intramuscular injection appears sooner than that of oral administration. The shortest period observed was twenty minutes, and three patients obtained marked relief after six, eight and ten hours respectively. We did not usually get such prompt results from patients using the enteric-coated tablets by mouth. I believe that peptone injected intramuscularly produces considerable reaction. No untoward reactions were noted in our patients receiving injections. I have not used the substance in giant urticaria. I thought it wise to restrict its use to the one condition for which I had adequate controls, and one which is easily recognized clinically and is readily measurable with regard to severity and duration. I know of its use for one patient with angioneurotic edema. This patient was comfortable, with great reduction in the edema during the time of administration of the tablets or the injections. However, the edema returned to its previous state from nine to fourteen hours after the cessation of injections or oral administration.

The Cholinergic Nervous System and Its Relation to the Thyroid Gland

DRS. A. R. MACLEAN, B. T. HORTON and A. C. DAVIS, Rochester, Minn.: It has been previously understood that sympathetic stimulation occurs in hyperthyroid states. It is our opinion that any sympathetic (adrenergic) stimulation that may occur in the hyperthyroid state is overshadowed by a stimulation of the parasympathetic (cholinergic) nervous system. The stimulation of the cholinergic nervous system of normal persons with acetyl-beta-methylcholine chloride (mecholyl produces signs and symptoms that simulate those of the hyperthyroid state. Persons who have hyperthyroidism have markedly increased sensitivity to this drug. Myxedematous patients appear to have a paralysis of this nervous system and an increased tolerance to mecholyl.

DISCUSSION

DR. LOUIS N. KATZ, Chicago: I wonder whether the authors are not carrying their interpretations too far. I am sure they know that mecholyl, like other cholinergic substances, not only stimulates the parasympathetic myoneural junctions but acts on all synapses in the peripheral ganglions in the autonomic nervous system. Because of this, the cholinergic substances in the animal and in man have not only a parasympathetic but also a sympathetic stimulating action. In addition, it has been shown that cholinergic substances bring about an outpouring of epinephrine. A cholinergic substance like mecholyl cannot be used to distinguish between parasympathetic and sympathetic stimulation. I should like to ask the authors whether they used atropine to prevent the manifestations from mecholyl and whether they have used prostigmine, a derivative of physostigmine, in patients with thyroid disease. Prostigmine acts to enhance cholinergic activity and gives less dramatic but more protracted effects.

DR. GRACE ROTH, Rochester, Minn.: I think Dr. Katz's criticism is well taken. I think the results should be taken only as a theoretical interpretation until more physiologic work is done, and care should be used in calling the stimulation either parasympathetic or sympathetic. However, in this study the basal metabolic rate was definitely increased by the subcutaneous injection of mecholyl.

DR. A. C. DAVIS, Rochester, Minn.: We realize that the interpretation which we have placed on our results is open to criticism from a number of angles. Of course it is rather difficult to say just why these patients overreact. Perhaps the reaction from hyperthyroidism is the same as overreaction of any kind—from nervous shock and many other nonspecific agents. However, it seems to us that the individual reaction to hyperthyroidism is similar to the reaction to an injection of mecholyl. With regard to Dr. Katz's question in reference to prostigmine and physostigmine, we have not used them in this connection.

Clinical Desensitization to Wheat with a Derivative of Acetylcholine

DR. EMMET F. PEARSON, Springfield, Ill.: Asthma, vasomotor rhinitis, eczema, urticaria and angioneurotic edema were reproduced in seven patients who complained of one or more of these symptoms by addition of wheat products to the diet. The symptoms subsided promptly on withdrawal of wheat. The same symptoms peculiar to the individual subject were reproduced at will by injection of approximately 10 mg. of acetyl-beta-methylcholine chloride (mecholyl). While wheat was eliminated from the diet, the patients were given daily injections of mecholyl in increasing doses from 0.5 mg., as tolerated by the patient. After from thirty to sixty days wheat was again added to the diet, and the original symptoms did not recur. In four of the patients previous attempts to desensitize with wheat extract had been unsuccessful. Symptoms have now been controlled for at least six months. It is postulated that repeated cholinergic stimulation alters the status of the bodily reactions so that a tolerance is gained for other stimuli.

Fatty Acids as Cholesterol Solvents in Bile

DRS. CLARENCE F. G. BROWN and RALPH E. DOLKART and K. K. JONES, PH.D., Chicago: Gallstones rarely form spontaneously in dogs, sheep, cats and rabbits. In contradistinction, in human beings, oxen and hogs biliary calculi occur frequently. Experiments carried on by means of shaking human gallstones in solutions of animal bile, bile salts and other mediums and by

direct insertion of human gallstones into the gallbladders of dogs demonstrated that greater dissolution occurred in the bile of dogs and sheep and less in the bile of human beings, oxen and hogs. Fractionation of the bile showed that the capacity of the bile as a cholesterol solvent could be isolated in the saponifiable or fatty acid fraction. This fraction was found to be high in the bile of the dog and sheep and significantly reduced in amount in the bile of animals which form gallstones. Repetition of the shaking experiments with tablets made of pure cholesterol confirmed the observation of greater activity of fatty acids as cholesterol solvents as compared with solutions of bile salts. It was found in addition that for each mixture of a specific bile salt with varying concentrations of a fatty acid there was an optimal concentration which if exceeded or not reached resulted in an inhibition of the rate of dissolution obtained with the fatty acid alone. Our data indicate that the cholesterol is held in solution in the bile by the fatty acids rather than the bile salts.

Calcium Balance in Thyroid Disease

DRS. ITALO D. PUPPEL, KARL P. KLASSEN and GEORGE M. CURTIS, Columbus, Ohio: Three normal persons maintained on a constant low intake of calcium remained in negative calcium balance. Four patients with exophthalmic goiter similarly maintained revealed an increased mobilization of calcium and a tremendous increase in excretion of this element through both the urinary and the gastrointestinal tract. Likewise, two patients with toxic nodular goiter showed an increase in excretion of calcium, but only slightly over normal. On the other hand, two patients with nontoxic nodular goiter remained in physiologic calcium balance. Increased feeding of calcium to a normal person on a low intake of calcium produced an immediate positive calcium balance. Similar increased feeding of calcium to a patient with hyperthyroidism resulted in a retention of calcium which was six times normal and a consequent positive calcium balance. One patient with exophthalmic goiter had shown an increase in the negativity of the calcium balance prior to subtotal thyroidectomy. Examination two years postoperatively revealed an absence of all characteristic symptoms and a basal metabolic rate of —9 per cent. Studies of calcium balance showed that the excretion of calcium was also normal and that the calcium balance had returned to within normal limits.

DISCUSSION

DR. RUSSELL M. WILDER, Rochester, Minn.: I have long believed, as has Aub, that the loss of calcium from the skeleton in hyperthyroidism is not to be explained by increased activity of the parathyroids, if for no other reason than that the level of calcium in the blood has never been found elevated. The observation of Drs. Puppel, Klassen and Curtis that calcium is excreted differently in toxic goiter, as compared to exophthalmic goiter, provides further support for the contention of Plummer that these two conditions are distinct entities. However, the evidence presented for a difference in the calcium balances is not entirely satisfactory, for the reason that the basal metabolic rate in the cases of toxic goiter was lower than in the cases of exophthalmic goiter. It would be desirable to compare patients with comparable basal metabolic rates.

DR. GEORGE M. CURTIS, Columbus, Ohio: Our determinations of the calcium balance of patients with thyroid disease have gone hand in hand with our studies of iodine balance. Ten years ago we set out to determine the total iodine balance in patients with hyperthyroidism. After the development of three successive methods for the biologic determination of iodine, this has been accomplished with fifteen patients, the majority having thyroid disease. At the same time we determined the total calcium balance. We wished to compare the two, owing to the close physiologic as well as clinical relations between the thyroid and parathyroid glands. A part of these combined studies have been reported (Puppel, I. D., and Curtis, G. M.: Calcium and Iodine Metabolism in Thyroid Disease, *Arch. Int. Med.* **58**:957 [Dec.] 1936). Others are being reported. It has been thought that exophthalmic goiter and toxic nodular goiter are two diseases. Nevertheless, some authors think that they are the same disease, the one representing a more acute manifestation of hyperthyroidism and the other a more chronic and hence more insidious form. The results which Dr. Puppel has presented reveal a difference between the calcium metabolism of exophthalmic goiter and toxic nodular goiter. Admittedly, this is a small series on which to base conclusions; nevertheless it is indicative and in accord with the work of others. The two patients with toxic nodular goiter had a lower average basal metabolic rate: + 28 per cent. The three with exophthalmic goiter had a higher rate, averaging + 40 per cent. Nevertheless, there appeared to be a difference in the management and utilization of calcium in the two diseases. Moreover, the iodine balance of these same patients revealed differences, giving further ground for regarding the two diseases as differing. The two patients with toxic nodular goiter showed a greater increase in the negativity of the iodine balance than the three patients with exophthalmic goiter. This in itself may not be so significant. Nevertheless, the increased excretion of iodine was greater in the urine of the patients with toxic nodular goiter and greater in the feces of the patients with exophthalmic goiter. In all we should consider these metabolic differences as indicative of corresponding differences between the two diseases. Comparing the disturbed iodine metabolism of patients with hyperthyroidism with the disturbed calcium metabolism of patients with hyperparathyroidism reveals a striking similarity.

Percutaneous Absorption of Estrogenic Substances by the Human Female, with Especial Reference to Growth of the Breast Induced by Local Application of Estrogenic Ointments

DR. CYRIL M. MACBRYDE, St. Louis: Several workers have produced local and general effects on the animal body by application of estrogenic substances to external surfaces. The application of appropriate amounts of the substances to any part of the skin has resulted in estrous changes and in mammary and uterine growth in certain spayed animals. DeFremery of Holland has reported that the best production of mammary growth in the virgin goat is accomplished by the application of estrogen directly to the skin of the udder. There are few studies of the effects of percutaneously applied estrogen in the human female, and there are no reports of the effect of estrogen directly applied to the breast to induce mammary development. Studies were performed on three women lacking mammary development and exhibiting signs of hypogonadism. Estrogenic ointments were found to induce unilateral mammary growth when only one side received applications of the active material and the other side was treated with the inactive ointment base. The results are shown by caliper measurements and photographs. Vaginal smears changed from inactive to the active estrous state, and characteristic changes were noted in the vulva as the result of the percutaneously absorbed estrogen.

DISCUSSION

DR. PAUL STARR, Chicago: I wonder whether Dr. MacBryde mentioned some work by Hans Selye on mechanical stimulation of the breast in order to produce lactation. Is it possible that the factor of mechanical stimulation of the breast was not thoroughly controlled? It was dramatically shown by Dr. MacBryde that after injection treatment was discontinued atrophy was extremely rapid. Was that also true after the inunction treatment?

DR. SAMUEL SOSKIN, Chicago: Dr. MacBryde's photographs are convincing. I do not think the members need doubt that he produced the results he reported. Nevertheless, I think it should be mentioned in a meeting of this sort that, while it may be permissible to produce a desirable effect by the use of estrogenic substance in a patient whose ovarian function is decreased or absent, one should not transfer such experiments to women with normal ovaries. It is well known that the prolonged use of small doses of estrogen may result in ovarian atrophy. It is also known that with larger doses one can get luteinization of the ovaries, which results in sterility and other phenomena. Therefore, one should be cautious about considering the use of such therapy in women in whom one wishes to preserve or improve ovarian function.

DR. CYRIL M. MACBRYDE, St. Louis: My work was purely experimental, and I hope the procedure will not be introduced into general practice until a great deal more study has been done. The limitations and dangers of estrogen therapy by inunction have not yet been clearly defined. In two patients who received the treatment I felt from my previous thorough study that there was probably no active ovarian tissue and so there

was no danger of injuring any possible gonadal function. In the third patient, who had some ovarian activity, I undertook the experiment with a great deal of trepidation. She has improved generally and has suffered no ill effects. However, I agree with Dr. Soskin that the use of estrogen in normally menstruating women and women with presumably normal ovaries may have great potential danger, especially with large doses such as I used. In answer to Dr. Starr about the effect of manipulation, I may say that as far as it was possible to determine there was exactly the same amount of mechanical stimulation on the two sides, but the breast which received the estrogenic ointment always grew at a much more rapid rate than the control breast. It is true that the breast will regress in size markedly and quickly after discontinuance of either injection or inunction. Whether treatment with the ointment causes a persistence in size of the breast for any greater length of time than the injection treatment I am not sure as yet.

Urinary Excretion of Androgens Following the Injection of Testosterone Propionate

DRS. E. PERRY MCCULLAGH and J. M. RUMSEY and W. KENNETH CUYLER, M.A., Cleveland: About 100 assays for urinary androgens are reported for sixteen men with hypogonadism and seven normal men. Single assays have been done in one group following single injections of varying doses, and the ratio of excretion to injection shown. Repeated assays for the same persons appeared to demonstrate diminished rates of excretion as injections continued. Single injections followed by daily assays for hypogonadal persons showed a prompt rise in excretion and a gradual fall to normal. With single doses of from 5 to 10 mg. the excretion of androgen rises to near or to within the lower range of normal, falling to previous levels within one or two days. With larger doses the elevation is much greater. With doses as high as 100 mg., relatively normal levels of excretion may be maintained for about five days. Single injections in a normal person caused a prompt rise followed by a distinct depression to below normal and finally a recovery of the original excretion rate in four or five days. If excreted androgens are calculated as androsterone, it is found that the amount of androgen which can be recovered from hypogonadal persons on the first day following injection of testosterone propionate is from 20 to 50 per cent of the injected quantity, whereas, if assays are done each day for five to seven days, quantities varying approximately from 25 to 75 per cent of the injected substance can be recovered.

Variations in Genital and Somatic Development with Bilateral Cryptorchidism

DRS. W. O. THOMPSON and N. J. HECKEL, Chicago: A study has been made of eleven males from 15 to 29 years of age with bilateral cryptorchidism. In no instance was somatic development completely normal. When both testes remained within the abdominal cavity there commonly resulted infantile genitalia, a high-pitched voice, long extremities, broad hips and absence of hair on the face and body. This was not uniform, as demonstrated by a normal-size penis in two cases in which neither testis could be palpated. In one patient with bilateral intra-abdominal testes genital growth was produced with anterior pituitary-like principle. Usually, however, growth could not be produced in such instances. Spermatogenesis was not observed in any patient, either before or during treatment with the anterior pituitary-like principle. Testes in the inguinal canal are more capable of function than those in the abdomen, as demonstrated by frequent growth of the genitalia in such instances, with and without administration of the anterior pituitary-like principle. Both testes can be completely normal only when they are in the scrotum. However, the interstitial cells may show a surprising degree of function even though both testes remain within the abdomen.

DISCUSSION

DR. PAUL STARR, Chicago: There seem to be a number of variants, one of which is the factor controlling the response of the testes to the substance, evidently specifically suited to stimulating it when the testis is normal. Do I understand that these studies indicate that the location of the testis in the abdomen renders it unlikely to respond to the anterior pituitary-like principle? How is it possible, then, that in children in whom the testis is in the abdomen the material produces the onset of puberty and the descent of the testis? If that criticism is just, is the difference in responsiveness of these patients a matter of age rather than of location of the testis?

DR. SAMUEL SOSKIN, Chicago: I should like to ask the authors to discuss some work reported six or eight months ago by T. W. Mimpriss (Treatment of Retention of Testis, *Lancet* **1**:533 [March 5] 1938), who presented evidence to show that if the testes were intra-abdominal the use of anterior pituitary-like principle, if it did not cause them to descend, might actually cause them to atrophy.

DR. E. P. MCCULLAGH, Cleveland: The authors have come to the conclusion that the reason for failure of response of the testes in these patients to injection of anterior pituitary-like principle is that they lie in an abnormal position in the body. This may be true in some degree, but I believe that an alternative explanation might be considered. Two types of relatively severe hypogonadism are seen clinically. In one type the remnant of testicular tissue can be detected in the scrotum, and all the symptoms can be accounted for on a basis of deficiency of activity of the testes themselves. In the other there may be obvious testicular hormonal deficiency, but, in addition, there are other signs which cannot be accounted for purely on a basis of testicular hormonal failure. The authors' cases of cryptorchidism are of this latter type. It seems fair to assume that, if the mechanism which is involved in the bringing of these testes into normal position is severely damaged, the testes may be subnormally developed as well as lying in a markedly abnormal position. Under such circumstances, may it not be possible that the development of the testes themselves may be altered by deficiency in this mechanism? If this is true and the mechanism which causes testicular descent is more nearly normal, then the testes should be more nearly normally developed, as well as lying closer to their normal position. Therefore, I suggest that the lack of response in cases of severe cryptorchidism might be more intimately connected with a deficiency in the factor which causes their development and descent than to actual position in the body per se.

DR. ELMER L. SEVRINGHAUS, Madison, Wis.: I should not want to minimize the position of the testis in its biologic response. I think there is an analogy in the position of the ovary. I have observed cases of primary amenorrhea or marked underactivity of the ovary which responded well to pituitary gonadotropic material. I have observed other cases in which there was little ability to respond to treatment with the same preparation. The ability to respond was measured by the intensity of the vaginal smear. Here one is dealing with an objective thing, the menstrual cycle, and it cannot be a matter of position because the ovaries function entirely within the abdomen. It must be something else, the ability of the gonad to respond to a given stimulation. Why do some ovaries never respond more than a little? There must be a similar problem in the testes. Unfortunately in the testes there is nothing to act as a measure of responding intensity except the size of the external genitalia.

DR. W. O. THOMPSON, Chicago: I am sure Dr. Starr did not understand what I said about location. In the boys I presented in whom we got a response to stimulation, one or both testes were either in the inguinal canal or deflected over the external oblique muscle, a position in which we think they are more responsive to stimulation. Mimpriss recently wrote an interesting article on the whole problem of undescended testes. I do not know whether his evidence that the anterior pituitary-like principle causes atrophy if the testis is incapable of response is adequately supported by the data he presented. One of the most interesting things that Mimpriss pointed out is that the only testes which came down with treatment were those which would have come down spontaneously at the time of puberty if no treatment had been given. We have come to that conclusion

independently as the result of a large number of observations over a period of about three years. Dr. McCullagh questioned the wisdom of concluding that the position of the testis accounts for its failure to respond to administration of gonadotropic substance. With this point of view I heartily agree. It is possible that the testes remained within the abdomen because of lack of development, or they may have undergone atrophy or been replaced by scar tissue as a result of remaining within the abnormal environment of the abdomen for such a long period. It would therefore be unwise to conclude that position alone was the responsible factor. Rather, the changes associated with or resulting from long-standing position of the testes in the abdominal cavity produce the results observed. Dr. Sevringhaus pointed out that in patients with underdeveloped ovaries striking response may be observed after the administration of the gonadotropic factor from the pituitary. He suggested, therefore, that not too much attention be paid to the position of the testis as a cause of failure of response. However, the situation is different in the two instances. The ovary is normally located in the abdominal cavity, while the testis is normally located within the scrotum. Absence of the normal environment is presumably the determining factor. It has been repeatedly demonstrated in both man and animals that, when testes which normally are in the scrotum are placed in the abdominal cavity, atrophy occurs and spermatogenesis ceases. In many instances normal size and function may be resumed if they are again placed in the scrotum.

Is the Potassium Tolerance Curve Specific for Detecting Adrenal Cortical Insufficiency in Disease?

DRS. JAMES A. GREENE and H. LEVINE, Iowa City: The potassium tolerance curve has been advocated as a method for detecting adrenal cortical insufficiency. Before it can be accepted as a diagnostic criterion its specificity for adrenal cortical insufficiency must be ascertained. We have obtained the potassium tolerance curve in a variety of maladies, and it was altered in certain cases of asthenia, bromism and edema. The first two conditions may be confused with early Addison's disease. Therefore the similarity of the manifestations of Addison's disease and bromism and the possible causes for alteration of the potassium tolerance curve in association with conditions other than Addison's disease are discussed.

DISCUSSION

DR. PAUL STARR, Chicago: Is it necessary to control the sodium chloride balance in these patients for some time before the test is given or is it sufficient to assume that a diet high in salt will do? Is it possible that patients with bromism had had an abnormally high potassium intake?

DR. JAMES A. GREENE, Iowa City: I cannot answer that question. In some cases of induced bromism we had to reduce the salt intake in order to induce bromism. In others we did not. Some patients were on a salt-free diet and others were on a general diet.

Measles Encephalitis

DRS. M. G. PETERMAN and M. J. FOX, Milwaukee: It is our opinion that measles encephalitis, or encephalomyelitis complicating measles, is an entity as distinct as is the encephalitis following vaccination against smallpox. We believe that the disease is an acute inflammatory lesion of the brain caused by an attenuated virus of measles which has accumulated in the brain in certain patients. This entity must be kept in mind by every physician who deals with measles. It may easily be recognized if it is kept in mind. On or about the fourth day after the appearance of the rash the child suddenly becomes drowsy, lethargic or comatose, or a convulsion may develop. Examination then reveals a comatose child with usually some degree of rigidity of the neck, dilated pupils and exaggerated reflexes. The blood count usually shows polymorphonuclear leukocytosis; the spinal fluid, pleocytosis, usually lymphocytic, an increase in globulin and a colloidal gold curve with the greatest change in color in the middle or meningitic zone (0123321000). The sugar content of the fluid is usually normal or elevated unless that of the blood is low. No further examinations are necessary or advisable to establish the diagnosis. There can be no question of interpretation of this clinical picture. In the matter of treatment we are convinced that good nursing care and symptomatic treatment constitute the limits of present therapy. As in poliomyelitis and all virus diseases, when the earliest symptoms are recognizable the virus has already completed an irreversible reaction with the nerve cells. There is no specific treatment, and the convalescent serum of measles cannot possibly be of value.

DISCUSSION

DR. JAMES A. GREENE, Iowa City: I should like to ask Dr. Peterman if he thinks the disease represents a secondary infection or a complication of measles. I studied mumps and found that encephalitis as a complication of mumps occurred frequently. I wonder whether the cases described were of the more severe type and whether the milder type was overlooked.

DR. LEE FOSHAY, Cincinnati: In view of the therapeutic results obtained by Dochez and his associates in distemper and by Tamura in venereal lymphogranuloma I do not think Dr. Peterman's therapeutic pessimism should be accepted in its entirety. There are both specific and nonspecific modes of treatment that modify the course of some virus diseases. I know it is often stated that treatment is of no avail in any virus disease, but I do not think this should hamper physicians in future trials of therapeutic procedures. I should like to ask the authors whether they think the recent use of human convalescent serum or of human placental globulin in attempted prophylaxis of the disease may have played any part in the apparent recent increase in the incidence of measles encephalitis.

DR. M. G. PETERMAN, Milwaukee: It seems to us that measles encephalitis is a definite entity; that is, the virus of the disease has invaded the nervous system. In that respect we may say it is a primary disease, and yet since it develops only with measles it must be a secondary infection. It apparently results from the same virus, with perhaps an accumulation in the brain. We have seen mild meningitis with all the mild infectious diseases. Scarlet fever often has its onset with convulsions. Pneumonia may be associated with meningitic symptoms, and there may be changes in the spinal fluid which promptly subside, and we consider the meningitis a secondary symptom complicating pneumonia, whereas in measles encephalitis we consider that the virus has produced the disease and then a secondary extension has produced another disease of the central nervous system. I doubt that any case of typical complete measles encephalitis could be overlooked because of the severity of the symptoms and the duration of the disease. I doubt that the meningeal irritations or the milder cerebral symptoms can be classified as encephalitis, because in all contagious diseases, particularly those mentioned as well as mumps, some mild cerebral involvement may occur. Young children particularly have cerebral involvement with many infections in which there is high fever. I am pessimistic about the use of convalescent serum, probably as an attempt to counteract the scientific salesmen from the convalescent serum centers. I have heard physicians remark "I had to give convalescent serum because the people demanded it." I think it should be understood that convalescent serum is of no value and has had no value in preventing encephalitis. After all, only approximately 60 per cent of the persons coming in contact with measles will have measles, and that depends entirely on the intimacy and the duration of exposure. It is difficult to evaluate statistics on prophylaxis against measles.

Focal Epileptogenic Lesions of Birth and Infancy and Their Eventual Radical Treatment

DRS. H. M. KEITH and WILDER PENFIELD, Montreal: This is a clinical study of patients who had craniotomy because of focal epileptogenic lesions which could be traced to injury at birth or in early infancy. The patients were carefully studied clinically, electrical explorations of the cortex were carried out at operation, and an attempt has been made to diagnose in retrospect the type of lesion that occurred at birth. Certain types of injury were found as follows: 1. Old fracture of the skull; laceration of the brain, hemorrhage and scar formation. 2. Subdural hemorrhage with resultant subdural adhesions and convolutional atrophy. 3. Cerebral atrophy due to thrombosis of a large artery. 4. Focal atrophy due to compression ischemia. 5. Diffuse atrophy due to natal asphyxia. 6. Adhesions and convolutional atrophy due to infantile meningitis.

Current Medical Literature

AMERICAN

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Titles marked with an asterisk (*) are abstracted below.

American Journal of Cancer, New York

34: 501-688 (Dec.) 1938

*Synovial Sarcomas in Serous Bursae and Tendon Sheaths. L. Berger, Quebec, Que.—p. 501.
Production of Primary Bone Tumors (Fibrosarcoma of Bone) by Intramedullary Injection of Methylcholanthrene. A. Brunschwig, Chicago.—p. 540.
The Production of a Melanotic Neoplastic Disease in Fishes by Selective Matings: IV. Genetics of Geographic Species Hybrids. M. Gordon and G. M. Smith, New Haven, Conn.—p. 543.
Carcinoma and Venous Thrombosis: The Frequency of Association of Carcinoma in the Body or Tail of the Pancreas with Multiple Venous Thrombosis. E. E. Sproul, New York.—p. 566.
Comparative Study of Ovaries and Other Endocrine Glands in Rats with Benign Transplanted Breast Tumors and in Normal Rats Injected with Sex Hormones. J. Heiman, New York.—p. 586.

Synovial Sarcomas.—From a study of five personal cases of synovial sarcomas and a review of the literature, Berger concludes that histologically only those tumors should be considered of synovial nature which present one or more specific features of the normal synovial tissue. From a topographic point of view his cases show that synovial sarcomas may arise outside of and far from articulations, in the midst of soft tissues, where they originate in serous bursae, normal or irregular from a purely anatomic point of view. With regard to evolution, synovial sarcomas are highly malignant tumors, although they seem at first to grow slowly. Synovial sarcomas of serous bursae apparently take a more rapid course than those of articulations. Recurrences develop in almost all patients operated on. Death is generally due to pulmonary, exceptionally to cerebral metastases. Definite cure is exceptional and can be obtained only by early removal. Therapeutic measures should therefore be prompt and radical.

American Journal of Clinical Pathology, Baltimore

9: 1-120 (Jan.) 1939

The Septic Syphilodermas. C. S. Butler.—p. 1.
History of Syphilis in 180 Patients in Which the Kline Tests, the Kolmer Test and the Kahn Test Are in Disagreement. J. H. Mills and Elsa Jahn, Baltimore.—p. 10.
Simplified Complement Fixation Technic for Serologic Diagnosis of Syphilis. F. Boerner and Marguerite Lukens, Philadelphia.—p. 13.
Tumor Nomenclature: Suggestions for Its Revision. H. E. Robertson, Rochester, Minn.—p. 24.
Changes in Serum Calcium, Inorganic Phosphate and Phosphatase Activity in the Pregnant Woman. M. Bodansky, with assistance of Katherine Campbell and E. Ball, Galveston, Texas.—p. 36.
*The Protective Action of Alcohol in Experimental Trichinosis. J. B. McNaught and G. N. Pierce Jr., San Francisco.—p. 52.
Nutritional Anemia, Clinical and Experimental Studies. R. M. Tyson, F. W. Konzelmann and H. C. Lennon, with technical assistance of Hanna Eymann, Philadelphia.—p. 58.
*Study of the Complement Fixation Reaction in Tuberculosis. J. A. Kolmer, Philadelphia, and J. F. Mahoney, Stapleton, N. Y., with assistance of Elsa R. Lynch.—p. 71.
The Criteria of a Dependable Basal Metabolism Report. P. Roth and Pearl E. Buckingham, Battle Creek, Mich.—p. 79.
The Goiter Cycle and Its Anatomic Findings: Report of 1,028 Sectioned Goiters. B. Markowitz, Bloomington, Ill.—p. 93.
Practical Classification of Leukemic and Related Conditions. V. H. Moon, Philadelphia.—p. 100.

Alcohol and Trichinosis.—Since there are reports that alcoholic beverages taken liberally with trichinous meat offers protection against infection and since the use of generous quantities of alcoholic liquors has been advised as therapy in trichinosis, McNaught and Pierce investigated this problem by in vitro studies and by experimentation on rats. Their conclusions are that while alcohol has little direct action on trichinella larvae in vitro and only halves the number of larvae which develop in the rat after a fixed dose of free Trichinella is ingested, it reduces the severity of the infection by 80 per cent if the alcohol is taken at the same time as is trichinous meat. A single dose of alcohol taken together with trichinous meat reduced the number of Trichinella that encysted in the muscles of rats by 80 per cent, but when alcohol was taken in large quantities over a period of seven weeks during the maturation, larval bearing, migrating and encysting stages of the parasites it gave no protection. In vitro experiments suggest that this protective action is due to the fact that alcohol interferes with the digestive liberation of encysted Trichinella. Experiments on rats verify this. The daily ingestion of from 6 to 8 cc. of absolute alcohol per kilogram of rat did not appreciably raise their blood alcohol values. Rats infected with Trichinella showed the highest blood eosinophilia during the third week of infection.

Complement Fixation Reaction in Tuberculosis.—Kolmer and Mahoney performed tuberculosis complement fixation tests on the serums of 408 tuberculous individuals; of these 63.7 per cent gave positive reactions with an 8 year old antigen of partially degreased human bacilli prepared and tested by the Kolmer method. The presence or absence of fever at the time the specimens of blood were collected had little or no influence on the results, since positive reactions were obtained in sixty-three of the febrile and 64.1 per cent of the afebrile cases. Four of twenty-five serums from syphilitic nontuberculous donors gave positive tuberculosis complement fixation reactions, presumably due to the fixation of complement by syphilitic antibody with the lipoids and waxes remaining in the partially degreased bacilli of the tuberculosis antigen. The authors recommend the performance of the Wassermann test on all serums submitted for the tuberculosis complement fixation test; when the former gives a positive reaction, great caution is required in the interpretation of a positive tuberculosis reaction.

American J. Digestive Diseases, Huntington, Ind.

5: 721-776 (Jan.) 1939

Studies on Humans with a New Secretogogue Meal. R. Upham and F. Spindler, New York.—p. 721.
Peptic Ulcer of the Esophagus. D. T. Chamberlin, Boston.—p. 725.
Food Allergy and Its Rationalization. H. C. Bradley and S. Belfer, Madison, Wis.—p. 730.
Pain in Carcinoma of the Stomach: Preliminary Report. A. B. Rivers and T. J. Dry, Rochester, Minn.—p. 732.
The Effect of Acetyl-β-Methylcholine (Mecholyl) on Gastric Secretion in Animals and in Man. J. Flexner and I. S. Wright, New York.—p. 736.
History and Development of Gastric Analysis Procedure. F. Hollander and A. Penner, New York.—p. 739.
Peptic Ulcer: Effect of High Protein Diet on Behavior of the Disease. C. Windwer and M. J. Matzner, Brooklyn.—p. 743.
Value of Gastroscopy in Diagnosis of Phytobezoar: Case Report. J. M. Ruffin and R. J. Reeves, Durham, N. C.—p. 745.
Ulcerative Colitis of Twenty-Eight Years' Duration with Recovery. W. Z. Fradkin, Brooklyn.—p. 746.
Treatment of Operable Rectal Cancer in Poor Surgical Risks. G. E. Binkley, New York.—p. 749.
*Practical Method of Analyzing the Precipitating Factors Producing Peptic Ulcer. E. J. Callahan and D. W. Ingham, Saratoga Springs, N. Y.—p. 751.

Factors Producing Peptic Ulcer.—It is evident to Callahan and Ingham from the cursory review of the current theories that despite criticism against the neurogenic origin it is yet the most constant etiologic factor in peptic ulcer. The food habits of a patient with ulcer must be carefully studied, as a well arranged, nonirritating, low residue diet is the foundation on which treatment is built. Although studies in heredity have not clearly demonstrated that there is a transmitted tissue susceptibility to peptic ulcer, this may be assumed because there seems to be a correlation between body build, personality and other qualities and this common gastrointestinal lesion. The authors employ an uncomplicated office procedure in their practice of gastro-enterology. They have constructed two charts each containing an equilateral triangle the sides of which are represented by the letters A B C. The hereditary factor is represented by A, the psychogenic factor by B and the food factor by C. One chart represents the diagnostic or analytic chart and is constructed with the apex of the triangle downward, which symbolizes imbalance. This demonstrates to the patient the mechanism of his recrudescences and recurrences by the ease with which this triangle is thrown

off balance. After a routine history and physical examination have been completed and a clinical diagnosis of peptic ulcer has been confirmed by fluoroscopic and x-ray examination, the first chart is shown to the patient. The cause of peptic ulcer may be projected on the sides of the triangle. The A side of the triangle is dismissed by explaining to the patient that he has an inherited susceptibility to peptic ulcer. The B side of the triangle may be divided into four main divisions: long illness in the family, financial troubles, unfaithful spouse and unexplained worry. The C side of the triangle, although the food habits of people with and without peptic ulcer are practically the same, is necessary to complete the hypothesis. After this survey has been made with the patient, the psychogenic factor is considered. The particular inciting agents responsible for the presenting complaint are elicited and identified. Careful and repeated questioning will reveal the psychic stimulus which by constant repetition produces the onset of his disease or a recurrence. A second chart is designated the therapeutic chart, in which the triangle is constructed with the base downward representing stability. The sides of the triangle are labeled in the same manner. Thus, the one factor which is within control is the food factor; hence it has been established as the base of the triangle. The remaining two sides are explained as follows: On the assumption that there is a hereditary trend in peptic ulcer the patient must accept this and try to live within this limit of ability. For example, if he is 25 per cent disabled by his disease he must strive to live 100 per cent of the 75 per cent and not more. The patient is urged to seek possible solutions for the anxieties which he may have. If the problem is of such magnitude that it cannot be dismissed with ease, he is cautioned to accept a philosophic view and do the best he can each day, be honest with himself and avoid fatigue and worry.

Journal of Lab. and Clinical Medicine, St. Louis

24: 337-448 (Jan.) 1939. Partial Index

Juvenile Diabetes Mellitus: Comparative Study of Standard Insulin, Crystalline Insulin, Protamine Insulin and Hexamine Insulin. H. M. Feinblatt, Brooklyn.—p. 337.

Atmospheric Pollen of Nashville, Tenn. Evangeline Bowie, Nashville, Tenn.—p. 342.

*The Effect of Copper and Iron on Secondary Anemia of Therapeutic Malaria in General Paresis. P. G. Schube, Boston, and B. D. Prescott, Hartford, Conn.—p. 346.

Studies in Bone Marrow. A. S. Gordon, Brooklyn.—p. 352.

Coronary Artery Thrombosis. F. J. Smith, B. E. Goodrich and R. J. Needles, Detroit.—p. 367.

Clinical Observations on Value of Various Xanthine Derivatives in Angina Pectoris. H. M. Massel, Chicago.—p. 380.

An Attempt to Mobilize Lipoids from Storage Depots by Deep Massage and Increased Tissue Temperatures. J. J. Short and J. D. Currence, New York.—p. 395.

Skin Reactions: VI. Simple Micromethod for the Assay of Histamine in Mammalian Blood. H. A. Abramson and I. Ochs, New York.—p. 398.

Photo-Electric Recording of the Pulse and of Other Oscillatory Movements with the Electrocardiograph. A. B. Hertzman, St. Louis.—p. 409.

Response to Liver Extract of Experimentally Induced (Typhoid) Anemia in Rabbits: Negative Result. A. J. Creskoff and T. Fitz-Hugh Jr., Philadelphia.—p. 411.

Refining of Antiserums: II. Improvements in Preparation of Refined and Concentrated Pneumococcus and Meningococcus Antibacterial Serums. E. Cardone and K. G. Falk, New York.—p. 417.

Use of Noncooked, Nonsterilized Coconut Milk as Additional Nutrient Substance in Culture Mediums. L. Blauvelt, Asheville, N. C.—p. 420.

Method for the Determination of Bromine in a Protein-Free Filtrate. Helen L. Wikoff, Eloise Bame and M. Brandt, Columbus, Ohio.—p. 427.

Copper and Iron in Anemia from Therapeutic Malaria.—In the course of their work on the treatment of dementia paralytica with malaria, Schube and Prescott often observed that the secondary anemias which almost invariably resulted were exceedingly alarming not only in their intensity but also in the persistence with which they remained after the termination of the malaria, and irrespective of the institution of ordinary iron or liver therapy. The combination of copper with iron was instituted in some of these cases, and the combination enhanced the formation of hemoglobin and erythrocyte. This was well illustrated in cases of secondary anemia of unknown origin, as the combination increased the hemoglobin and erythrocytes quite consistently in most instances. The hemoglobin and erythrocytes were both depressed in secondary anemia induced by malaria in dementia paralytica patients but untreated with copper or iron and increased only many weeks after the termination of the malaria. When ferrous iron was administered regularly from the time of the malarial inoculation to the return of the blood picture to normal, the average curves of depression and the return of the blood elements to normal were approximately the same. But in the same type of patients when copper and iron were regularly administered from the time of the malarial inoculation to the return of the blood picture to normal the curve dropped slower, and before it had dropped half the distance of the other two groups it began to rise again and reached normal much sooner than those of either group. The time from the first temperature elevation to the lowest hemoglobin and erythrocyte counts was usually shorter, and the return to normal was generally more rapid. This lessened severity of the anemia coupled with the fact that it was more difficult for the malaria to produce the anemia and the fact that the erythrocyte counts and hemoglobin were rapidly restored to normal by means of copper and iron would indicate that these minerals are of value in combating the anemia incurred by malaria. Iron and copper did not interfere in any way with the expected therapeutic benefit from the malaria, with the temperature rises or with the action of tryparsamide. The authors feel that copper and iron can be used with impunity in dosages much larger than the ones (32 mg. of ferrous iron and 1 mg. of copper orally in capsules) they used. It is highly probable that larger doses would be more satisfactory. They believe that their work indicates that the reticulo-endothelial system of man can be stimulated to such an extent that it can minimize the devastation wrought in the blood stream by malaria. It also indicates that the malaria did not materially affect the reticulo-endothelial system of the cases studied and thereby intensify the anemia produced by direct erythrocyte destruction.

Journal of Nutrition, Philadelphia

17: 1-102 (Jan.) 1939

Comparative Study of Metabolism of Certain Amino Acids, with Special Reference to Respiratory Exchange and Heat Production. M. Kriss, State College, Pa.—p. 1.

Level of Inorganic Phosphorus in the Blood of Dairy Cattle. S. R. Johnson, State College, Pa.—p. 15.

The Factor I (Vitamin B_6) Requirement of the Rat. Mildred K. Dimick and C. B. Schreffler, Emeryville, Calif.—p. 23.

Effect of Yeast and of Thiamin on Production of Low Iodine Goiter. P. L. Harris and R. E. Remington, Charleston, S. C.—p. 31.

Acid Soluble Phosphorus Content of Muscle of Rats Under Various Diet Modifications. H. C. Struck, C. I. Reed and Jeannette L. Cohen, Chicago.—p. 35.

Effects of High Humidity on Skin Temperature at Cool and Warm Conditions. H. Freeman and B. A. Lengyel, Worcester, Mass.—p. 43.

Effect of Chondroitin Sulfuric Acid on Gizzard Erosion and Growth in Chicks. L. A. Crandall Jr., F. F. Chesley, R. E. Gray and H. E. Robinson, Chicago.—p. 53.

Secondary Deficiency of Vitamin B_1 and Riboflavin in the Blacktongue Producing Diet. L. H. Margolis, G. Margolis and Susan Gower Smith, Durham, N. C.—p. 63.

Digestibility of Raw Potato Starch in Man. J. M. Beazell, C. R. Schmidt and A. C. Ivy, Chicago.—p. 77.

Diet and Rate of Depletion of Hepatic Vitamin A. E. J. Lease and H. Steenbock, Madison, Wis.—p. 85.

Biologic Value of Carotene in Various Fats. E. J. Lease, Jane G. Lease, H. Steenbock and C. A. Baumann, Madison, Wis.—p. 91.

Missouri State Medical Assn. Journal, St. Louis

36: 1-48 (Jan.) 1939

Fractures of Both Bones of the Leg. F. A. Jostes and M. B. Roche, St. Louis.—p. 1.

Fractures of the Os Calcis. D. C. McKeever, Kansas City.—p. 7.

Highway Accidents: Early Management of Fractures. M. L. Klinefelter, St. Louis.—p. 10.

Vision and Its Relation to Automobile Accidents. P. S. Luedde, St. Louis.—p. 14.

American Red Cross Highway Emergency First Aid Station Program. A. W. Cantrell, St. Louis.—p. 16.

Motor Mishaps and the Medical Profession. H. D. Griffith, Jefferson City.—p. 18.

*Hemorrhoids: Study of Series of Cases Improved by Conservative Treatment. G. L. Krause, St. Louis.—p. 20.

Artificial Fever Therapy: Report on Three Years Clinical Experience. L. Bromberg, St. Louis.—p. 24.

Hemorrhoids.—Krause injected from 5 to 10 minims (0.3 to 0.6 cc.) of 5 per cent phenol in sterile olive oil or 5 per cent quinine and urea hydrochloride in the treatment of seventy-five cases of hemorrhoids; the ages of the patients ranged from 16 to 86 years. The injection was made around and above the hemorrhoid just beneath the mucous membrane. Chronic con-

stipation was complained of generally. Bleeding, pain and protrusion was a universal complaint. Itching occurred in 60 per cent of the cases, of which ten cases showed pruritus. The interval between injections varied from five to ten days, bleeding persisted in every case until the last ulcerated site had disappeared; for this reason the ulcerated spot was always chosen for the first injection. Symptoms of pain, bleeding and protrusion invariably improved following the first and second injection. Pruritus with itching was the most resistant condition and was the last to disappear. The patient is cautioned not to strain or defecate within from twelve to twenty-four hours after the injection. Seventy-one patients were ambulatory with normal activity restricted.

Ohio State Medical Journal, Columbus

35: 1-120 (Jan.) 1939

An "Autologous Fascia Suture" Technic in Surgical Treatment of Direct Inguinal and Femoral Hernia. R. C. Austin, Dayton.—p. 17.
Clinical Aspects of Peripheral Vascular Disease. H. C. Eddy, Cleveland.—p. 21.
Nutritional Anemias of Infancy and Early Childhood. C. V. Moore, St. Louis.—p. 25.
Incidence and Diagnosis of Cardiovascular Syphilis. C. F. Garvin, Cleveland.—p. 34.
*Use of Benzedrine in the Depressed Phase of the Psychotic State. L. A. Dub, Columbus, and L. A. Lurie, Cincinnati.—p. 39.
Treatment for Acute Conjunctivitis. A. L. Schonberg, Cleveland.—p. 46.
Surgical Management of the Diabetic Patient. A. T. Bowers and T. P. Sharkey, Dayton.—p. 48.
Hemorrhoidectomy, with Special Reference to Postoperative Care and Complications. C. C. Perry, Cleveland.—p. 54.
Cooperation by the Roentgenologist and Otolaryngologist. E. R. Hargett, Springfield.—p. 58.
Scleroderma: Report of Case Treated with Acetyl Beta Methylcholine Chloride (Mecholyl) Iontophoresis. F. A. LeFevre, Cleveland.—p. 60.

Amphetamine in Depressed Psychoses.—Dub and Lurie selected, for treatment with amphetamine sulfate, forty-eight depressed female patients from a service of about 1,500 patients at Longview Hospital because of their pronounced depression as revealed by their mood, speech and actions. The ages of the women ranged from 18 to 75 years. They had been institutionalized for from ten months to twenty-six years. The patients were given 5 mg. of amphetamine sulfate twice a day. The first dose was given at breakfast and the second with the noon meal. To those patients who refused to take the medication the drug was mixed with the food. In certain cases the dosage was increased to 10 mg. twice a day. This was done if there was no improvement after a week's trial on the smaller dose. The medication was continued for three weeks. A lactose placebo was then substituted without the knowledge of the attendants or patients. The placebo was continued for three weeks, after which no medication was given for two weeks. Following this rest period the patients were again given the placebo for four weeks, after which amphetamine sulfate was again substituted and continued for six weeks. The effects of the treatment on the appetite, thirst, pulse, sleep, mood and psychomotor activity were recorded daily. Weight and blood pressure were recorded weekly. Forty-two of the women showed definite improvement when amphetamine was administered. A patient was considered benefited if she showed improvement in at least two of the following criteria: weight, cooperativeness and psychomotor activity. During treatment with the placebo, five patients became so violent that they could no longer participate in the experiment. Only five of the remaining forty-three patients maintained their initial improvement, while thirty-eight relapsed when the lactose placebo was substituted for the amphetamine. During the rest period of two weeks, three more patients were lost to the experiment, one through discharge as apparently cured and two because they became violent. Of the remainder, six remained improved while thirty-four remained unimproved. When the patients were again placed on placebo treatment only three held their gains. In other words, at the end of this period 92 per cent of the patients in this series were practically in the same mental condition that they had been in at the beginning of the experiment. But when amphetamine was again administered an immediate and striking improvement was observed in thirty-five, while only six failed to respond. An equally striking slump was observed when the amphetamine therapy was again discontinued, the results being practically the same as those during the rest period. The best response was obtained in the paranoid and patients suffering from cerebral sclerosis, while the patients with dementia praecox responded the least. The duration of the disease seemed to have no bearing on the results obtained. Age, however, seemed to be of some significance as the women from 41 to 60 years of age showed the highest incidence of improvement.

Public Health Reports, Washington, D. C.

54: 29-58 (Jan. 13) 1939

Undergraduate Engineering Training in Public Health and Related Activities in Engineering Colleges of the United States. A. P. Miller.—p. 29.
*Evaluation of Odor Nuisance in the Manufacture of Kraft Paper. J. M. Dalla Valle and H. C. Dudley.—p. 35.
Amblyomma Philipi: New Tick from Texas and Mexico, with a Key to Known Species of Amblyomma in the United States (Acarina: Ixodidae). R. A. Cooley and G. M. Kohls.—p. 44.

Odor in Manufacture of Kraft Paper.—There are three types of obnoxious odors due to the process of manufacturing kraft paper. Dalla Valle and Dudley list them as (1) hydrogen sulfide, (2) volatile organic sulfur compounds and (3) chemical smoke containing sodium sulfate, sodium sulfide, traces of hydrogen sulfide and quantities of carbon and organic materials. Hydrogen sulfide is formed and released to the atmosphere at smelter furnaces where molten sodium carbonate and sodium sulfide are dropped into water and in the separator building in which this solution is filtered. The treatment of the fresh wood chips by the digester liquor containing sodium sulfide brings about the formation of many unknown volatile organic sulfur compounds. At nearly all points of the process at which the pulp is handled after the digestion, certain of these ill smelling volatile organic compounds are liberated. The greatest volume and concentration of these compounds are released from the turpentine condenser as steam is led from the digester tanks and when the pulp is blown from these tanks with the release of large quantities of steam containing many volatile constituents. The large quantities of smoke which are released through exhaust stacks release large amounts of sodium carbonate in a colloidal state. Although sodium carbonate in a pure state is odorless, much uncarbonized organic matter accompanies these particles, traces of hydrogen sulfide and various volatile oils of unknown composition. These organic materials, which are at least partially adsorbed on the colloidal particles of sodium carbonate, give rise to the peculiar odor when this smoke is blown across the ground. Methods of study are recommended which may lead to the control of the odor-generating processes. The possibilities of electrical precipitators to prevent an excess of chemical smoke are stressed.

Radiology, Syracuse, N. Y.

32: 1-130 (Jan.) 1939

*Lipoid Pneumonia in Infants and Children. R. S. Bromer and I. J. Wolman, Philadelphia.—p. 1.
*Bronchogenic Carcinoma: Study of Eight Autopsied Cases. W. E. Howes and S. G. Schenck, Brooklyn.—p. 8.
Spontaneous Mediastinal Emphysema: Report of Case Associated with Spontaneous Pneumothorax. J. B. Morey, Ada, Okla., and M. C. Sosman, Boston.—p. 19.
Corelation of Physical and Clinical Data in Radiation Therapy. W. H. Meyer, New York.—p. 23.
X-Ray Rentals in Hospitals: Analysis of Current Rental Costs in Hospitals and Medical Buildings. L. H. Garland, San Francisco.—p. 46.
Multiple Heteromorphologic Malignant Tumors of the Uterus. H. W. Jacox, G. Major and Margaret R. Baker, Pittsburgh.—p. 51.
Researches in the Problem of Radium Poisoning and Tolerance Dose of Radium. B. Rajewsky, Frankfort on the Main, Germany.—p. 57.
Value of Radiation in Treatment of Carcinoma of the Breast. L. G. Allen, Kansas City, Kan.—p. 63.
Further Study on Direct and Indirect Actions of Radiation on Malignant Cells: I. Transplantation of Tissue Cultures of Mouse Sarcoma 180 After Exposure to Roentgen Rays: II. Cultures of Tumors Irradiated in Vivo. K. Sugiura and I. Cohen, New York.—p. 71.
Roentgen Diagnostic Importance of Adipose Tissue. J. Silbermann, Vienna, Austria; translation by E. T. Leddy, Rochester, Minn.—p. 77.
Relation Between Radiation Quality Factors and Depth. A. Mutscheller, New York.—p. 87.

Lipoid Pneumonia in Infants and Children.—Bromer and Wolman studied twenty-seven cases of lipoid pneumonia at the Children's Hospital. Twelve of these were found in a series of 137 consecutive necropsies. Of the twenty-seven

patients, twenty-two died and postmortem studies were performed on twenty. The nature of the pulmonary lesion was recognized in only one, although roentgenograms of the chest were made of sixteen. In two thirds of the cases the pneumonia was associated with some sort of constitutional debility (prematurity, rickets, congenital syphilis, microcephaly, infantile scurvy, mongolism, spastic diplegia, amyotonia congenita, intestinal malformations or congenital cardiac defects). This indicates that physical weakness must be considered as an important predisposing factor of lipoid pneumonia. Retardation of growth and poor nutrition, attributable in most instances to the constitutional disturbance rather than to the pneumonia, was present in twenty-one patients. The most common single symptom was chronic cough, present in six patients. As a rule the chest on physical examination seemed clear, although in a few instances minor signs were observed over the consolidated areas. None of the patients had a positive tuberculin test. The distribution of the pulmonary lesions at necropsy clearly indicated the exogenous origin of the lipoid. The posterior dependent portions of the lungs, and especially the perihilar regions, were always affected. The right lung was more involved than the left, possibly because of the straighter course of its main bronchus. The nodules and solid lobules of lipoid pneumonia were confluent, grouped or widely separated. Bands of scar tissue were sometimes present. The bronchopulmonary nodes were involved in a few instances. The roentgenograms of this series of patients, some showing a wide distribution, others an extremely slight involvement, emphasize the diverse x-ray variations. The pulmonary lesions can be classified as mild, moderate or severe, according to the extent of the involvement. This division is not dependent on the time that has elapsed following the aspiration of the oily substance or on the kind of oil aspirated. Experimental production of lipoid pneumonia as reported in the literature suggests that cod liver oil causes an acute pneumonia which, after subsiding, leaves residual foci, whereas liquid petrolatum produces a more chronic reaction, which should result in an unchanged appearance in the serial roentgenograms. The extent of involvement depends on the quantity of oil in the lung, regardless of whether it is aspirated in a single large amount or in repeated small quantities. The roentgenograms of the patients having only a mild involvement show an increase both in degree of density and in extent of the hilar shadows. The linear markings of the pulmonary fields are more exaggerated than normal. If small scattered areas of increased density are present they are usually situated along the descending branches of the right bronchus. The cardiac shadow obscures the left hilar markings. In the group with moderate involvement there is greater density of the perihilar shadows with widening in all directions. The dense shadows spread more or less homogeneously in all directions from the hilus. In several cases the left lung was unaffected. In the severe cases the perihilar shadows spread well out toward the peripheries of the lungs, although usually a clear zone is left between the dense shadow and the walls of the chest. As the child grows, this clear zone becomes wider unless the aspiration of oil continues. The edges of the lesions are either sharply demarcated or feathery. A definite lobar pneumonia shadow is not seen unless nonlipoid pneumonia is present simultaneously. Coincident inflammation of the lungs was found frequently at necropsy. This may develop in the mild, moderate or severe cases. Serial roentgenograms are necessary to recognize its development and also to establish the chronicity of the process when no pneumonia supervenes. The positive diagnoses made in the five patients of the series who are still living were based on the x-ray observations, typical of severe involvement and proved chronic by serial roentgenograms.

Bronchogenic Carcinoma. — Howes and Schenck report the pathologic features of eight fatal cases of bronchogenic carcinoma submitted to postmortem examination. Of the 737 new cases admitted to the Brooklyn Cancer Institute during 1937 there were seventeen of bronchogenic carcinoma, an incidence of slightly less than 3 per cent. In larger series of cases, bronchogenic carcinoma shows an incidence as high as 10 per cent of all cancers. The cause is still unknown, but it is generally conceded that some form of chronic pulmonary irritation accounts for the development of the neoplasm in most instances. The symptoms are not unlike those observed in other chronic pulmonary diseases, especially tuberculosis, bronchiectasis, pulmonary abscess, mediastinal tumor and fluid cyst of the lung. X-ray study, including the instillation of iodized oil, reveals the true nature of the pulmonary pathologic changes in the majority of cases. In the presence of pleural fluid which obscures the underlying markings of the lungs, overpenetrated films or Potter-Bucky exposures should be made. With a mass in the region of the thoracic aorta, kymographic studies are indicated to exclude the possibility of an aneurysm. A necrotizing process in the lung, portrayed roentgenologically, does not exclude the possibility of a carcinoma which has undergone necrotic liquefaction. A negative bronchoscopic examination does not preclude the diagnosis of a primary pulmonary tumor, especially when the involvement is in the upper lobes or located in the finer bronchi. If the diagnosis is in doubt, biopsy of an available enlarged lymph node or mass should be performed. A metastatic process may present the first symptom of the disease. Clinically the skeletal system, regional lymph nodes and pleurae are the sites of metastatic predilection. In the osseous system the pelvis, femur, spine, skull and ribs are the more susceptible regions. Roentgenologically the skeletal lesions show osteolytic, osteoblastic or combined types of involvement. The majority of patients with bronchogenic carcinoma die within one or two years. The present recognized forms of treatment are irradiation and surgery. Irradiation with the present technic is at best palliative; surgery offers hope in selected cases. Microscopically three types are recognized—the squamous carcinoma, the adenocarcinoma and an undifferentiated group.

Texas State Journal of Medicine, Fort Worth

34: 585-658 (Jan.) 1939

*Differential Diagnosis and Treatment of Anemias. E. E. Osgood, Portland, Ore.—p. 591.
Monocytic Leukemia: Report of Two Cases. W. N. Powell, Temple.—p. 595.
The Problem of the Diagnosis of the More Common Blood Dyscrasias. W. L. Marr, Galveston.—p. 599.
Tumors of the Ankle. W. G. Stuck and D. A. Todd, San Antonio.—p. 603.
Injuries of the Knee Joint. V. L. Tuck, Sherman.—p. 607.
Induction of Labor by Rupture of Membranes. A. T. Stewart, Lubbock.—p. 610.
Vomiting of Pregnancy: Its Prophylaxis and Treatment. Evelyn G. Powers, Amarillo.—p. 614.
Delay as a Factor in Obstetric Treatment. F. B. Smith, Houston.—p. 617.
The Problems of the Deaf. J. J. Shea, Memphis, Tenn.—p. 619.
Whose Responsibility Is Public Health and Medical Service? A. T. McCormack, Louisville, Ky.—p. 624.

Diagnosis and Treatment of Anemias.—Osgood states that the diagnosis of anemia should always be based on an accurate erythrocyte count and hemoglobin determination, since the symptoms of pallor, weakness, dizziness, shortness of breath and edema may be produced by other diseases and are absent in some cases of anemia. It is important to determine the reticulocyte count, the icterus index and the urobilinogen excretion in the urine in any case of anemia. If the reticulocyte count is above 4 per cent it indicates an increased rate of erythropoiesis and if below 4 per cent it indicates a decreased rate of erythropoiesis. An icterus index above 6 or the presence of clinical jaundice with a positive urobilinogen test in a dilution of 1 to 20 in the urine indicates an increased rate of hemoglobin destruction within the body if disease of the liver or obstruction of the biliary tract can be excluded. An icterus index below 4 indicates a decreased rate of erythrocyte destruction. Anemias should be classified as macrocytic, hypochromic, microcytic or normocytic by an accurate determination of the color, volume and saturation indexes. There is no longer a place for the old terms "primary" and "secondary" anemias, since all anemias are secondary to some usually determinable cause and intelligent treatment can be given only when this cause is determined and removed. Correct diagnosis is a prerequisite to intelligent therapy.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Medical Journal, London

1: 1-50 (Jan. 7) 1939

The Problem of High Blood Pressure in Man. G. W. Pickering.—p. 1.
Prolonged Injections of Male Sex Hormones into Normal and Senile Male Rats. V. Korenchevsky and K. Hall.—p. 4.
Sulfanilamide Treatment of Guinea Pigs Infected with Brucella Abortus. G. S. Wilson and Irene Maier.—p. 8.
*Clinical Observations with Stilbestrol (Diethylstilbestrol). W. R. Winterton and T. N. MacGregor.—p. 10.
*Therapeutic Trials of Diethylstilbestrol. A. A. Loeser.—p. 13.
Vitamin D in Diet: Palatable Methods of Supply. Jessie Lindsay and V. H. Mottram.—p. 14.
Symmetrical Peripheral Gangrene in Cardiac Failure. C. B. Perry and T. B. Davie.—p. 15.

Clinical Observations with Synthetic Estrogen.—Winterton and MacGregor treated forty-five patients complaining of symptoms referable to an endocrine disturbance and six others in whom it was considered desirable to inhibit lactation with the synthetic estrogenic compound diethylstibestrol. The responses obtained were similar to those which would have been expected from treatment with natural estrogen. Oral administration of the synthetic substance was found to be as effective as intramuscular therapy. Some of the patients experienced slight nausea during the treatment, but in only one was the treatment poorly tolerated.

Therapy with Synthetic Estrogen.—Loeser used a synthetic estrogen (diethylstilbestrol) in the treatment of fifteen patients with minor degrees of ovarian insufficiency: climacteric disorders, dysmenorrhea, hypo-oligomenorrhea, secondary amenorrhea, ovarian insufficiency and pruritus vulvae. The synthetic estrogen shows such definite estrogenic effects that it has a good substitution action in various forms of ovarian insufficiency. In six of the fifteen cases for which it was used, unpleasant secondary effects such as nausea or vomiting were produced.

Journal of Mental Science, London

85: 1-184 (Jan.) 1939

Revaluation of Psychiatry. D. K. Henderson.—p. 1.
Diffuse Sclerosis with Preserved Myelin Islands: Pathologic Report of Case, with Note on Cerebral Involvement in Raynaud's Disease. B. Horanyi-Hechst and A. Meyer.—p. 22.
Social Values in Mental Hospital Practice. W. J. T. Kimber.—p. 29.
Truancy. J. M. Partridge.—p. 45.
Resultant and Purposive Psychiatry. H. Crichton-Miller.—p. 82.
A Death During Insulin Treatment of Schizophrenia: Pathologic Report. S. A. MacKeith and A. Meyer.—p. 96.
Insulin Therapy: Unusual Hypoglycemic Sequels in Two Psychotic Patients, with Observations on Glycemic Levels. W. M. F. Robertson and G. L. Ashford.—p. 106.
Preliminary Inquiry into the Part Played by Character and Temperament in Accident Causation. E. G. Chambers.—p. 115.
Some Considerations of the Physical Factor in Delusional States. R. E. Hemphill.—p. 119.
*Note on Agglutination Reactions in Typhoid Carrier State. J. R. Murray and F. Partner.—p. 126.

Agglutination Reaction in Typhoid Carriers.—Murray and Partner performed Widal tests on twenty-five known typhoid carriers. Eleven of these carriers gave negative blood agglutination reactions at a time when the organism of typhoid could be recovered from the stools. The authors state that a greater number of carriers will be detected if bacteriologic studies of the stools are always made. In this connection attention may be drawn to the long persistence of the passage of organisms; one person in the series dates the original infection to 1910.

J. Royal Inst. Public Health and Hygiene, London

1: 887-950 (Dec.) 1938

The Rise and Fall of Certain Diseases Concurrently with the Progress of Hygiene and Sanitation. S. Woodwark.—p. 897.
Review of the Medical Supervision of Industry by the State. J. C. Bridge.—p. 911.
Development and Progress of Methods of Combating the Bedbug. V. Borland.—p. 923.
Treatment of Arthritis in the Home. F. M. Hilliard.—p. 932.
The New Maternity Services from the Point of View of the Obstetric Surgeon. A. L. Robinson.—p. 937.
Physical Recreation for Women and Girls. H. M. Watt.—p. 945.

Lancet, London

2: 1503-1554 (Dec. 31) 1938

Hypotension and Flying. A. F. Rook and D. J. Dawson.—p. 1503.
Rolling Disease: New Syndrome in Mice Associated with Pleuropneumonia-like Organism. G. M. Findlay, Emmy Klieneberger, F. O. MacCallum and R. D. Mackenzie.—p. 1511.
*Detection of Horse Serum (Meningococcus Antitoxin) in Blood and Cerebrospinal Fluid. J. M. L. Burtenshaw.—p. 1513.
Miles's Abdominoperineal Operation: Treatment Before and After. S. O. Aylett.—p. 1516.
Macrocytic Anemia of the Achrestic Type: Case Described. G. M. Wauchope and M. Leslie-Smith.—p. 1518.
*Treatment of Subacute Bacterial Endocarditis with Sulfapyridine. G. R. Ellis.—p. 1521.
Pericarditis Associated with RT Deviation Without Tamponade. A. Morland and J. Osborne.—p. 1522.

Horse Serum in Blood and Cerebrospinal Fluid.—Burtenshaw tried to find what proportion, if any, of therapeutic serum, administered parenterally to patients suffering from meningococcic meningitis, reached the cerebrospinal fluid. Since there is no simple method of assaying meningococcus antitoxin, it was thought that a test for the presence of the antitoxin-containing horse serum in the body fluids of subjects injected with the serum would furnish at least an indication of the presence of antitoxin. Such a test was provided by an adaptation of the precipitin reaction. Twenty-three patients with meningococcic meningitis and one from whom only a strain of staphylococcus was isolated received meningococcus antitoxin only by parenteral, usually intravenous, injection. Horse serum protein was detected in the cerebrospinal fluid in every one, though its concentration varied greatly from case to case and was always small compared with the simultaneous concentration in the blood. The values of the ratio horse serum in blood/horse serum in cerebrospinal fluid agree well with the observations of Freund for typhoid antibodies. Allott (1938) in a large series of cases, including the twenty-four of this investigation, finds similar variations of sulfanilamide content in the cerebrospinal fluid in spite of equivalent dosage, but in contrast to the behavior of horse serum the sulfanilamide concentration in the cerebrospinal fluid rapidly approximates, during the first twelve hours after administration, that in the circulating blood. There is no apparent correlation between age and the permeability of the blood-brain barrier to horse serum, though this barrier may have varied with the intensity of the meningitis. Traces of foreign protein persisted for a long time, both in the blood and in the cerebrospinal fluid. Intrameningeal injections of serum ensure the immediate presence of large amounts of antibody at the site of infection; yet equally striking is the steepness of the drop in serum concentration from the heights reached by intrameningeal dosage. Within one or two days, however large the dose, the cerebrospinal fluid serum content has fallen to the low levels attained by parenteral administration alone.

Treatment of Endocarditis with Sulfapyridine.—Ellis obtained much improvement in two cases of subacute bacterial endocarditis with sulfapyridine. The pyrexia in the first case was controlled in twenty-four hours by 2 Gm. of sulfapyridine. The profound fall in temperature that can be produced by large doses makes the author wonder whether some temperature-reducing mechanism may not be at work other than the mere destruction of organisms. The fall in temperature is at least in part presumably due to a sterilizing of the blood stream, though there is as yet no certain proof of this. Obviously the ideal investigation which must be undertaken is daily blood cultures while the patient is apyrexial under the influence of the drug. As the dosage of sulfapyridine was reduced in the two cases cited, the temperature slowly rose, but it did not reach its former heights until the drug was practically stopped. It may be that there is partial sterilization of the blood, but not of the primary focus of infection, the endocardium. It seems that the mechanical problem of the locked up streptococci is still the stumbling block in the treatment of this type of endocarditis. Sulfapyridine is none the less, as far as the author is aware, the only drug which has ever been known definitely to reduce the temperature and temporarily to improve the clinical condition.

Bruxelles-Médical, Brussels

19: 323-360 (Jan. 8) 1939

*Benign and Malignant Hypertension: Their Relations to Kidney. E. Dicker.—p. 323.
Primary Abdominal Pregnancy: Case. M. Vastesaeger and G. De Tœuf.—p. 333.

Benign and Malignant Hypertension.—Dicker, in discussing the pathogenesis of benign and malignant hypertension, reviews studies of other investigators and describes his own clinical and experimental observations. Summarizing the present status of the question he says that: 1. The diminution of the irrigation of one or both kidneys suffices to induce a hypertension of long duration, without renal insufficiency. 2. The hypertension that is secondary to renal ischemia does not have a nervous origin but is due to a humoral action. 3. The vascular modifications that are observed in a man with benign hypertension and which consist essentially in a thickening of the media are the same as those which can be observed in dogs that have had hypertension for a long time but do not show renal insufficiency; thus they are secondary to hypertension and the late result of the renal intervention. 4. Renal insufficiency alone never determines hypertension or anatomopathologic changes of the vessels. 5. The necrotic lesions that are pathognomonic of malignant hypertension are the result of renal insufficiency developing unexpectedly in the course of an old hypertension. The kidney being responsible for the hypertension, it can be affirmed that in the last analysis the vascular changes are likewise the result of a renal intervention. Thus it can be seen to what extent the role assumed by the kidney is essential in the pathogenesis of hypertension. It remains to be determined what is the substance (or the complex of substances) which, originating from an ischemic kidney, is capable of producing a definite hypertension either directly or indirectly by means of endocrine products; finally it remains to be seen whether it is the same as that which, in case of renal insufficiency, is capable of bringing about necrosis of the arterioles and of transforming a benign hypertension into a malignant one.

Presse Médicale, Paris

47: 57-80 (Jan. 14) 1939

*Physiologic and Clinical Significance of Peroxidasic Action of Blood. M. Polonovski and M. Jayle.—p. 57.
Cerebrospinal Concussion. F. Pedrazzini.—p. 58.

Peroxidasic Action of Blood.—In studying the biochemical mechanism of oxidation in human blood, Polonovski and Jayle show that the phenomena of oxidation are dependent on three types of enzymes: the dehydrogenases, the oxidases and the peroxidases. They demonstrate that there exist in human blood, apart from the peroxidases of the leukocytes, two peroxidasic systems. The first is the peroxidasic system A; its activity is related to 1 cc. of plasma and expressed in iodine units (I. U.). The second is the peroxidasic system B, "the hemoglobin activator of the plasma"; it is expressed by the same symbol and is related to 0.1 cc. of plasma. In a table the authors compare the values for A and B in several healthy persons and in patients. From the biologic point of view, hemoglobin reveals itself as an animal peroxidase of catalytic action which is in all points comparable to that of vegetable peroxidases and like them capable of playing a part in the biologic oxidations of the tissues. From the clinical point of view, the existence and the pathologic variations of the hydro-alkyloperoxidase of the plasma (A) and of the plasmatic activator (B) of the peroxidasic action of the hemoglobin permit certain prognostic deductions. The difference between A and B, which is normally positive, becomes in certain disorders the more negative as the prognosis becomes more unfavorable.

Strasbourg Médical

98: 475-490 (Dec. 5) 1938. Partial Index

*Late Results of Stellectomy in Bronchial Asthma. R. Leriche and R. Fontaine.—p. 475.
Differential Arteriographic Diagnosis Between Arterial Embolism and Acute Thrombosis. R. Fontaine and P. Branzen.—p. 479.

Stellectomy in Bronchial Asthma.—From 1926 to 1934 Leriche and Fontaine resorted to stellectomy in fourteen cases of bronchial asthma. In order to evaluate the late results of the operation, eleven patients were followed up for some time. In seven cases in which unilateral stellectomy was performed, the asthmatic crises immediately disappeared in two cases but the operation failed in five. Up to the present, the satisfactory results of unilateral stellectomy in one case have lasted for thirteen years (recovery) and in the other the crises, greatly attenuated, reappeared after a period of seven years of complete cessation of the attacks. In four cases of bilateral stellectomy the operation was followed by immediate disappearance of the asthmatic crises. In one case, recovery has lasted up till now (seven and a half years after the operation). In the other three cases the crises reappeared greatly attenuated both in frequency and in intensity. The satisfactory results in the last three cases have lasted from three to five years after the operation. The authors state that the preliminary infiltrations of the stellate ganglion before stellectomy is of value in attenuating or arresting the development of asthmatic crises while the patients are being prepared for stellectomy. Generally, but not in all cases, the patients who have a favorable reaction to the preliminary infiltration of the stellate ganglion have also a favorable response to stellectomy. They point out the dangers and lack of satisfactory results of other surgical treatments (vagotomy or resection of the posterior bronchial plexus) which are resorted to by some authors in the treatment of bronchial asthma. They emphasize the satisfactory results of bilateral stellectomy, especially in intractable forms of bronchial asthma. The operation involves a simple technic and is well tolerated by the patients and is dependable for immediate and late results.

Schweizerische medizinische Wochenschrift, Basel

69: 25-44 (Jan. 14) 1939. Partial Index

Prognosis of Mental Disturbances. B. Dukor.—p. 25.
Nature of Gout and Its Relation to Rheumatism, Chronic Articular and Other Diseases. E. Stotzer.—p. 29.
*Treatment of Acute and Chronic Diarrheas with Salt-Free Diet. H. Salomon.—p. 31.
Simulated Pregnancy: Case. W. Neuweiler.—p. 32.

Treatment of Diarrhea with Salt-Free Diet.—Salomon shows that the treatment of diarrhea has undergone considerable changes in recent decades. Whereas formerly it was the rule first to remove the "materia peccans" by means of purgatives, it is now believed that the intestine purges itself sufficiently in the course of a severe diarrhea. The author says that he as well as others have long defended this opinion, because the administration of purgatives in the course of diarrhea may have serious results. He further cites the experiments with tea and fruit juices which he carried out in 1909, the experiences which Heisler and Mora made with the apple cure and other observations. He agrees with von Noorden's opinion, according to which the absence of sodium chloride is the essential factor in the fruit diet as well as in other measures that prove effective in diarrhea. He cites clinical histories to prove that the salt-free diet is effective in diarrhea. If the salt-free diet is employed in diarrhea, it should be carried out along lines similar to those employed in nephrosis. Sweet foods are especially desirable; the sugar replaces the salt to a considerable extent. The fluid intake should consist chiefly of fruit juices and indifferent mineral waters. Discussing the action mechanism of the salt-free diet in diarrhea, the author shows that it is readily understandable on the basis of the laws of osmosis.

Archivios Argentinos de Pediatría, Buenos Aires

9: 611-739 (Dec.) 1938. Partial Index

Banti's Disease: Late Results of Splenectomy; Case. E. A. Beretervide and S. Mindlin.—p. 611.
*Erythema Nodosum and Pulmonary Tuberculosis: Cases. L. Rascovsky and A. Rascovsky.—p. 625.
Septicemia, Abscess of Kidney and Perinephric Phlegmon in Newborn Infant. D. A. Giraldes.—p. 636.

Erythema Nodosum and Pulmonary Tuberculosis.—The Rascovskys report six cases of erythema nodosum in children ranging in age from 4 to 9 years. The condition developed in the course of a febrile attack similar to grip, during which the patients had a cough without any sputum. Four patients had a history of contact with patients who had pulmonary tuberculosis. The clinical examination for pulmonary tuberculosis gave negative results in three cases and positive results in three. The Mantoux test gave strongly positive results in all cases except the third, which became positive during aggravation of

the febrile and pulmonary symptoms. Roentgenograms were taken in the course of the febrile attack during which erythema developed. They showed secondary tuberculous infiltration at the hilus of the lung in three cases, secondary infiltration around the hilus in one case and primary infection in another. One of the patients was apparently in good health, but since the father had pulmonary tuberculosis a roentgenogram was made of the child's thorax, which showed the presence of a typical primary complex of recent development at the upper lobe of the lung. Three years later erythema nodosum developed three months after measles. Roentgenograms made in the course of the disease showed that the primary complex was entirely calcified. Two of the patients in the group developed allergic hypersensitivity and asthma within a year after the erythema disappeared but which improved after desensitization.

Archiv für Dermatologie und Syphilis, Berlin

178: 201-372 (Dec. 19) 1938. Partial Index

Epidermophyton Luteum and Its Variants. S. Szathmáry.—p. 216.
Clinical Aspects and Histology of Anonychia. J. Alkiewica.—p. 234.
*Demonstration of Granular Formations of Type of Virus Elementary Bodies in Efflorescences of Patients with Pemphigus. S. Wolfram. —p. 240.
Oxidation-Reduction Potential and Reducing Processes in Living Skin. G. Radaeli.—p. 253.
Dermatofibrosarcoma Protuberans. C. H. Beek.—p. 260.
Capillaroscopy and Capillarophotograms of External Male Genitalia. W. Schönfeld.—p. 276.

Virus Elementary Bodies in Pemphigus.—Wolfram gives a brief survey over the efforts that have been made to detect an infectious causal agent of pemphigus and thinks that the supposed agent probably belongs to the invisible viruses rather than to the bacteria. At his request a search was made for virus bodies in pemphigus blisters at Gerlach's institute. When this investigation gave positive results, the author decided to study all cases of pemphigus seen in his clinic for the presence of virus bodies. Investigations were made on eight cases of pemphigus and on six cases of dermatitis herpetiformis Duhring. Staining with victoria blue and with the primulin method was done in all cases. If the outcome was the same with the two stains, the results were regarded as positive provided the other criteria were fulfilled. The positive results of specimens that were stained according to Paschen's method or with Morosow's silver stain were accepted as valid only if at least one or both of the first two staining methods gave the same results. In all examined cases and in the majority of the examined specimens, granular formations were detected which were in every respect like the virus elementary bodies of the virus infections.

Archiv für Gewerbepathologie, Berlin

9: 179-294 (Dec. 21) 1938. Partial Index

Chronaximetric Examinations Before and After Work in Lead Workers and in Persons Who Have No Contact with Lead. H. J. Schütz.—p. 198.
Changes in Heart and in Blood Vessels of Lung During Experimental Silicosis and Silicotuberculosis. G. Hegemann.—p. 228.
Investigations on Causes and Prophylaxis of High Incidence of Pneumonia in Industrial Plant Producing Alloys for Refined Steel. M. Gundel and W. Heine.—p. 248.
*Vascular Diseases After Poisoning with Mercury. K. Fellinger and F. Schweitzer.—p. 269.

Vascular Diseases After Mercury Poisoning.—Fellinger and Schweitzer report the clinical histories of three patients in whom severe vascular impairments developed in connection with mercury poisoning. To be sure it is justifiable to inquire whether the vascular lesions are actually the result of a mercury intoxication or whether their concurrence with mercury poisoning is merely accidental. Although positive proof is lacking, many factors militate for a causal role of the mercury poisoning. In all three cases the vascular lesions developed at a time at which, although the early signs of mercury poisoning had disappeared, the chronic manifestations and sequels (dental lesions, tremor and psychic changes) were completely developed. This appearance at a time when late lesions and sequels develop seems to indicate that the vascular changes belong to the other manifestations of mercury poisoning, the more so as the chronological connection is similar to that which is observed in lead poisoning, in which vascular impairments are comparatively frequent. Moreover it appears improbable that, in comparatively young and hitherto entirely healthy persons, vascular lesions should develop with great rapidity, when it is considered that Raynaud's and Buerger's disease generally develop at first insidiously, causing only minor symptoms. These and other considerations make it probable that these vascular lesions and their sequels have a causal connection with the mercury poisoning. It was impossible to make anatomic studies on the vessels of the three patients with mercury poisoning, but the clinical manifestations of the vascular lesions resemble those of the various forms of obliterating endarteritis; however, in their unusually rapid, almost fulminant, course they differ from idiopathic vascular diseases.

Klinische Wochenschrift, Berlin

17: 1825-1856 (Dec. 24) 1938. Partial Index

Reduction of Respiratory Basal Metabolism in Defects of Right Side of Heart. A. Sylla.—p. 1829.
*Pathogenesis of Essential Hypochromic Anemia. W. Thiele.—p. 1835.
Recent Results with Conglobation Reaction for Tuberculosis According to Haag and Niggemeyer. F. E. Haag.—p. 1836.
Case of Addison's Disease on Traumatic Basis. R. Sichler.—p. 1839.
Determination of Arsenic in Cerebrospinal Fluid After Administration of Organic Arsenic Preparations. Vonkennel and Kimmig.—p. 1840.
Epinephrine Effecting Inhibition of Resorption in Alimentary Alcoholemia. B. Siegmund.—p. 1842.
*Therapy of Nontropical Sprue. H. W. Hotz.—p. 1843.

Pathogenesis of Essential Hypochromic Anemia.—Thiele directs attention to an anemia of the hypochromic type which frequently concurs with achlorhydria or achylia and occasionally with atrophies of the pharyngeal and esophageal mucosa. Moreover, it is often accompanied by koilonychia and by paresthesia, and it develops chiefly in women between the ages of 20 and 40. As regards the etiology of this form of anemia the opinions are still divided, but the role of the stomach has been discussed repeatedly. Those who investigated the problem of postoperative anemias have pointed out that the precipitated evacuation of the stomach plays an important part in the pathogenesis of these anemias. The author noted that in essential hypochromic anemia the gastrointestinal passage is almost regularly excessively accelerated. The evacuation of the stomach and of the upper portion of the small intestine is so rapid that after an hour the jejunum is empty and the chyme is already in the ileum. The author shows that the accelerated gastrointestinal passage of essential hypochromic anemia must be regarded as peculiar to this disease and the question arises whether this accelerated passage leads to disturbances in the resorption. He cites several investigators who are of the opinion that an accelerated passage of the ingesta through the small intestine impairs the resorption. The resorption of iron takes place chiefly in the duodenum and, so it may be concluded that only a part of the iron content of the food is utilized during the accelerated transport in patients with essential hypochromic anemia. The author cites animal experiments made by M. B. Schmidt which demonstrated that hypochromic anemias produced by iron deficiency increase in severity in successive generations. This was explained as resulting from the depleted iron depots in the maternal organism. In this connection the author points out that essential hypochromic anemia often shows familial appearance. Moreover, it has been observed in families in which other members had pernicious anemia, achlorhydria or achylia. Deficiencies in acidity and ferments are often detected in the female forebears of patients with anemia. The author reasons that children from mothers who have an impaired intestinal resorption probably inherit a subnormal iron storage, although they may not develop anemia. It may be assumed that this deficient iron depot is incapable of coping with extraordinary demands such as menstruations and pregnancies and so it is explained why essential hypochromic anemia appears chiefly in women.

Therapy of Nontropical Sprue.—Hotz says that it is not justified to regard the prognosis of nontropical sprue as entirely unfavorable. He shows that, although complete cure is rare, a suitable therapy will produce in the majority of cases freedom from symptoms. To be sure, since relapses are frequent the patients must remain under the supervision of the physician. Of twenty-two patients who were observed and treated

by the author, four were cured, thirteen were so greatly improved that they were able to resume their work, and five died of complications. The treatment requires much patience on the part of the physician as well as of the patient and it necessitates hospitalization. It consists chiefly in dietetic measures and in the administration of liver extracts. The intake of fats and carbohydrates should be reduced, but proteins, vegetables and fruits should be given in generous amounts. The liver extract must be given in large doses for a long time by parenteral administration. As soon as remission of the anemia is obtained, the liver therapy should be combined with oral and, if necessary, with intravenous administration of iron. With the administration of adrenal cortex extract and of yeast, a treatment which Verzár recommended for nontropical sprue, the author obtained no results which even approximately compared with those obtained by his own dietetic and liver therapy.

Problemy Tuberkuleza, Moscow

Pp. 1-184 (No. 9) 1938. Partial Index

Thoracoscopy and Thoracocautery in Pulmonary Tuberculosis. N. G. Stoyko.—p. 10.
*The Origin, Course and Therapy of Tuberculous Lobitis. B. P. Zvonnikov.—p. 26.
Roentgenologic Appearance of Disappearance of a Cavity. K. V. Pometsov.—p. 49.
Roentgenologic Demonstration of Fresh and Old Cavities. A. Ya. Rabinova.—p. 60.
Healing of Tuberculous Cavity. T. N. Oleneva.—p. 69.

Tuberculous Lobitis.—According to Zvonnikov, lobitis in the majority of cases is a manifestation of a primary infiltrating flare-up of the tuberculous process. Three factors play a part in the formation of a lobitis: the interlobar septum as the point of origin, local sensitization of the pulmonary tissue and a partial atelectasis accompanying the inflammatory process. Correct topographic diagnosis is arrived at through oblique and frontal roentgenograms. Diagnostic errors are committed principally in the cases of tuberculous lobitis with an acute onset. The differential diagnosis includes nonspecific pneumonia, cancer of the lung and lobar atelectasis. The prognosis of tuberculous lobitis is governed by two contrary tendencies. On the one hand the process tends to remain limited to the lobe for a long time; on the other, it displays an early tendency to break down and form cavities. Spontaneous recovery is possible but is extremely rare. Regressive alterations in favorable cases are those of resorption, scar formation or gradual resorption with disappearance of the interlobar septum. The therapy of lobitis is collapse. Artificial pneumothorax or phrenic exeresis is recommended for the acute cases and thoracoplasty for the old fibrocavernous forms. In the author's material artificial pneumothorax gave a satisfactory clinical effect in 48 per cent of the cases and phrenic exeresis in 21 per cent. The relative effectiveness of the two methods, however, cannot be arrived at from these figures because of the dissimilarity in the gravity of the cases.

Acta Orthopaedica Scandinavica, Copenhagen

9: 115-233 (Nos. 2-3) 1938. Partial Index

*Plastic Operations in Loss of Thumb. K. H. Köster.—p. 115.
Subtrochanteric Osteotomy in Relatively Old Congenital Luxation of Hip, Arthritis Deformans and Coxa Vara. E. Platou.—p. 132.
Some Cases of Transplantation After Orell's Method. W. Risinger.—p. 152.
Congenital Pseudarthrosis of the Leg. K. Stenport.—p. 181.
*Different Types of Tuberculosis of Hip in Children. G. Odelberg-Johnson.—p. 197.

Plastic Operations in Loss of Thumb.—Köster shows that extreme conservatism is necessary in operations on the thumb. If in spite of this it becomes necessary to amputate a thumb though the metacarpus is preserved and the carpometacarpal joint is mobile, it is advisable to mobilize the metacarpus by phalangization, a fissure being formed between the first and the second metacarpus. The author reports three cases in which this operation was successful. Descriptions are given of some of the numerous forms of plastic operations on the fingers, such as finger substitution of Lucksch and the plastic operations on the fingers according to Nicoladoni. These operations, aside from being technically difficult, rarely produce the desired results; that is, free mobility of the transplanted parts. Phalangization is the easiest operation, it rapidly produces a useful finger and it answers the demands which must be made on a finger substitute: strength, motility and sensitivity.

Tuberculosis of Hip.—Odelberg-Johnson reports seven cases of tuberculous coxitis in children, illustrating the following types of this disease: (1) coxitis with primary destruction of the acetabulum, (2) coxitis with primary luxation, (3) focus in the neck of the femur with perforation into the joint and (4) sequestration of the capital epiphysis. It is pointed out that in the early stages of tuberculous coxitis weight put on the extremities as well as muscular contracture may contribute to the deformity of the atrophic bony components of the joint and also to the development of bone destruction in adjacent parts of bones. Moreover, "extra-articular pseudarthrosis" usually develops after coxitis in early childhood and this morbid condition often is the final stage of infantile coxitis with primary luxation.

Ugeskrift for Læger, Copenhagen

100: 1367-1396 (Dec. 8) 1938

Climacterium in Men. L. Andresen.—p. 1367.
*Treatment of Retention of Testis with Special Regard to Hormonal Treatment and Indications for It. E. Guldberg.—p. 1368.
*Some Cases of Apicitis. H. Rasmussen and T. Meyer.—p. 1375.

Treatment of Retention of Testis with Special Regard to Glandular Therapy and Indications for It.—Guldberg advocates the institution of glandular therapy at the age of 10 in all cases of uncomplicated retention of the testis and in cases complicated with hernia. He says that if the treatment is not effective it will not lessen the chance for successful operative treatment and often considerably improves it. This view, he affirms, is supported by his results in the seven cases reported in which glandular therapy was given, in three instances followed by operative treatment. Cases in which the testis is fixed by stenoses in the inguinal canal, adherences and so on are considered unsuited for endocrine treatment; they call for operation and later glandular therapy if needed. Glandular therapy is contraindicated in cases of malignant degeneration and ectopia, also in cases with threatening incarceration of the testis, which might increase to a fateful degree on glandular therapy. A complicating hernia may by rapid growth or incarceration indicate early operation regardless of the patient's age; in these cases one must try to avoid such changes in the anatomic conditions as might hinder a later spontaneous descent of the testis or a descent effected by glandular therapy.

Some Cases of Apicitis.—Eight cases are reported, six in children from 6 to 12 years of age. In seven the diagnosis of apicitis was verified roentgenologically, in one only at necropsy. Rasmussen and Meyer state that the clinical symptoms vary greatly and may be vague or entirely absent and that only x-ray examination establishes the presence of a destructive process in the apex. There was paresis of the abducens nerve, together with characteristic pain in three cases, in two of which the paresis set in on the thirtieth and forty-sixth day respectively; in one there was double vision from the first day of the otitis. Five patients, including two of those with paresis of the abducens, had increased cell count in the spinal fluid. In three instances pronounced changes in the apex were manifest on the first x-ray examination on the eleventh, eighteenth and twenty-first day respectively of the apicitis; in the other four, marked changes appeared on later examinations. That the apicitis was accompanied by sphenoid sinusitis in five cases points to the advisability of careful examination of the sphenoid sinus in apicitis. In the first fatal case Ramadier's operation failed because there was not enough space between the carotid canal and the promontory to allow access to the apex. Operation on the apex with evacuation was done in four cases on the twelfth to the thirty-eighth day, in two by Ramadier's method. In all four there were soft cells in the apex with granulations or pus. One of these patients died from meningitis after a revision operation. The remaining three patients, two with marked processes in the apex, recovered although only ordinary chiseling was performed, with emptying of the perilabyrinthine cells. The author feels that more definite guides are needed for the treatment of apicitis, also for the time for operation.